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PNEUMONIA AT THE PHILADELPHIA GENERAL HOSPITAL, 1936-1946*

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PHILADELPHIA

IN RECENT years pneumonia has rapidly become less important as a cause of death. There has been a sharp decline in admission of patients with pneumonia in most hospitals and recent studies on the effectiveness of modern therapy of pneumonia have indicated a low case mortality. Nevertheless, at the Philadelphia General Hospital, pneumonia remains a serious problem, and the impression has been obtained that in late years the response of patients with pneumonia to specific therapy has not been so dramatic as that observed in earlier years. The present study was projected to verify this impression, and to determine if possible the responsible factors.

MATERIAL

The records of adult patients discharged from the Philadelphia General Hospital with the diagnosis of primary pneumonia in three representative years were studied. The year from July 1, 1936, to June 30, 1937, was one in which specific therapy was not available; the year from July 1, 1940, to June 30, 1941, saw the widespread use of sulfonamides; and in the year from July 1, 1945, to June 30, 1946, penicillin was available as an adjuvant to or substitute for the sulfonamides.

In an effort to exclude secondary pneumonias, consideration was restricted to patients less than sixty years of age. Cases of tuberculous pneumonia and postoperative and terminal pneumonia were also excluded. In all other patients, the final recorded clinical or pathological diagnosis was employed.

Patients treated in the special pneumonia wards of the hospital, except when admitted *in extremis*, had routine laboratory studies comprising sputum culture, blood culture and complete blood counts. These data are not complete in many cases treated in other wards. Typing of pneumococci was done routinely in 1936–37 and 1940–41 but, in 1945–46, only on pneumococci isolated from blood or exudates. The later years of the study saw increased use of x-ray examination on admission. Other data included the duration of illness and the type of medical care prior to admission, the maximum fever and the incidence of complications. The case mortality rates were calculated both for all admissions and for admissions of patients surviving twenty-four hours. The number of febrile days in the hospital, as well as the total hospital stay of recovered patients, was determined as a further indication of the therapeutic response.

FREQUENCY OF PNEUMONIAS ACCORDING TO DIAGNOSIS

The total number of cases studied was 368 in 1936–37, 540 in 1940–41 and 420 in 1945–46 (Table 1). In each year approximately 95 per cent or more of the cases were classified as lobar pneumonia or bronchopneumonia. Other bacterial pneumonias, caused by *Klebsiella pneumoniae*, streptococci, staphylococci, *Haemophilus influenzae* and Salmonella comprised 4.0 per cent of the total in 1936–37, 1.3 per cent in 1940–41 and 1.4 per cent in 1945–46. The diagnosis of viral pneumonitis was made in single cases in 1936–37 and 1940–41, but in the 1945–46 season, similar diagnoses, in this report grouped as viroid pneumonias, were made in 14 cases, or 3.4 per cent of the total for the year.

Analysis of the clinical and laboratory characteristics of the two major groups, lobar pneumonia and primary bronchopneumonia, revealed lesser differences than are commonly considered to exist between these two types (Table 2). It appears that the distinction was made in most cases on the basis of the x-ray or pathological report, for the other characteristics did not seem to vary sufficiently to permit a sharp differentiation of the groups. The differences were rather constant, however, in each of the years: patients diagnosed as having bronchopneumonia had a somewhat higher mean age, a slightly longer mean duration of symptoms, slightly less fever and a less marked leukocytosis on admission; sputum culture slightly less often demon-

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strated pneumococci, and positive blood cultures were less frequent in the bronchopneumonias. The frequency of higher types of pneumococci was greater also in this group. The case mortality tended to be higher in the bronchopneumonias, and among the recovered patients in this group the duration of fever and hospitalization tended to be less. It appears that the differences between primary lobar pneumonia and bronchopneumonia in each of the years under study were slight and that the two groups showed parallel changes from one year to the other. These observations indicate the difficulty of clinical differentiation and support the modern tendency to classify the pneumonias on an etiologic basis.

Although on this basis it seems justifiable to combine the two groups for purposes of further analysis, this has not been done since the criteria for diagnosis of primary bronchopneumonia are poorly defined and are not uniformly applied in all localities. Lobar pneumonia, on the other hand, is commonly considered to be a well defined entity, generally and uniformly recognized. For this reason, the remainder of this investigation is confined to patients with the diagnosis of lobar pneumonia.

The 261 patients with lobar pneumonia in 1936–37 received merely supportive treatment with the exception of 5 cases in which serum therapy was employed. In all respects the clinical and laboratory characteristics of the whole group are typical of those reported in the extensive American studies made before the introduction of serum therapy.[1] The mean age of thirty-five years and nine months, the mean white-cell count of 20,300 on admission and the case mortality of 23.3 per cent are noteworthy because of the changes in these characteristics noted in ensuing years.

In 1940–41 there were 429 patients with lobar pneumonia, 20 of whom failed to receive sulfonamides because of erroneous diagnoses on admission. Sulfadiazine was used in 184, sulfathiazole in 174 and sulfapyridine in 51 patients. Five patients received serum in addition. The sharp decline in the case mortality — to 5.4 per cent — is typical of that reported in studies made in the early years of sulfonamide therapy.[2, 3] Also notable in the 1940–41 season were the slightly increased mean age of the patients, the reduction in white-cell count and the short duration of fever after admission — the temperature was normal within forty-eight hours of admission in 57.6 per cent of patients receiving specific drug therapy.

There were 312 patients with lobar pneumonia in 1945–46. In 10 cases specific therapy was not received. Sulfadiazine alone was employed in 119 patients, a sulfadiazine-sulfamerazine combination in 34 patients, penicillin alone in 36 patients and penicillin in addition to sulfonamides in 113 patients. Nevertheless, the case mortality failed to show a further decline but rose slightly. The mean age of the patients rose sharply, and leukocytosis was significantly less marked. There was a distinct increase in mean duration of fever and of hospitalization; the incidence of patients who were afebrile in forty-eight hours was only 39.0 per cent. This was true regardless of the type of therapy used in the hospital. The case mortality varied in a remarkable fashion according to the therapy employed: patients receiving sulfonamides alone had a rate of 1.4 per cent, whereas those receiving penicillin had a rate of 12.0 per cent. This is not inconsistent with the excellent results obtained with penicillin in controlled studies and is merely an indication that all patients recognized as seriously ill received penicillin.

The rise in case mortality of lobar pneumonia observed in 1945–46 is not statistically significant when treated by the chi-square method, but it is remarkable in view of the additional availability of penicillin. There is ample evidence for the effectiveness of penicillin in lobar pneumonia, and the rise in mortality cannot be attributed to the use of penicillin instead of sulfonamides. Actually, the apparent slight increase in mortality was probably not due to chance but rather, as demonstrated below, to alterations in the age distribution of the patients. However, the patients with lobar pneumonia in 1945–46 showed a highly significant difference, the probability that the result was due to chance

TABLE 1. *Primary Pneumonias by Diagnosis among Patients under the Age of Sixty.*

DIAGNOSIS	JULY 1, 1936–JUNE 30, 1937		JULY 1, 1940–JUNE 30, 1941		JULY 1, 1945–JUNE 30, 1946	
	NO. OF PATIENTS	NO. OF DEATHS	NO. OF PATIENTS	NO. OF DEATHS	NO. OF PATIENTS	NO. OF DEATHS
Lobar pneumonia	261	80	429	43	312	38
Bronchopneumonia	91	31	103	15	87	12
Pneumonia due to Friedländer bacillus	2	2	6	5	1	1
Streptococcal pneumonia	7	2	—	—	1	0
Staphylococcal pneumonia	3	0	1	1	2	0
Influenzal pneumonia	3	2	—	—	2	1
Salmonella pneumonia	—	—	—	—	1	1
Viroid pneumonia	1	0	1	0	14	0
Totals	368	117	540	64	420	53

TABLE 2. *Clinical and Laboratory Characteristics of Lobar Pneumonia and Primary Bronchial Pneumonia.*

DIAGNOSIS	No. of Cases	Mean Age	Mean Duration of Illness before Admission	Mean Temperature on Admission	Mean White-Cell Count on Admission	Pneumococci in Sputum	Other Bacteria in Sputum	Patients with Pneumococcemia	Type of Pneumococcus					X-Ray Report of Lobar Pneumonia	X-Ray Report of Broncho-Pneumonia	X-Ray Report of Pneumonia Unclassified	Mean Duration of Fever in Hospital*	Mean Hospital Stay*	Case Mortality	
									I	II	III	IV	OTHER						TOTAL	CORRECTED†
		yr.	days	°F.	x10³	NO. OF CASES	NO. OF CASES							NO. OF CASES	NO. OF CASES	NO. OF CASES	days	days	%	%
Lobar Pneumonia																				
1936–37	261	35.9	4.4	103.5	20.3	160	16	33	27	18	15	2	107	42	2	50	5.8	22.4	30.7	23.3
1940–41	429	36.9	3.6	103.1	17.5	314	23	59	62	14	43	29	180	107	3	77	3.5	14.4	10.0	5.4
1945–46	312	39.5	4.6	102.9	13.9	206	17	26	5	13	12	1	8	135	5	126	5.3	17.7	12.2	6.5
Bronchopneumonia																				
1936–37	91	41.6	5.7	103.0	16.1	43	5	7	3	0	4	1	37	3	30	19	5.1	25.2	34.0	16.7
1940–41	103	42.0	4.4	102.5	13.9	47	8	3	3	0	7	6	50	3	34	32	3.0	12.6	14.6	11.1
1945–46	87	39.9	5.3	102.5	12.6	35	5	0	0	0	6	0	1	4	25	40	4.3	16.1	13.8	9.6

*Among patients who recovered.
†Corrected by exclusion of patients who died within twenty-four hours of admission.

TABLE 3. *Influence of Age in Lobar Pneumonia.*

AGE	No. of Patients	Mean White-Cell Count	Patients With Positive Blood Culture	Case Mortality		Mean Duration of Fever†	Patients Afebrile in Forty-Eight Hours†	Mean Hospital Stay†
				TOTAL	CORRECTED*			
yr.		x10³		%	%	days	%	days
1936–37:								
10–19	39	17.9	5	5.1	2.6	7.7	—	20.5
20–29	45	19.8	5	17.8	11.9	5.1	—	21.0
30–39	70	20.0	8	24.3	19.7	5.5	—	23.5
40–49	55	22.7	6	36.3	27.1	5.4	—	23.2
50–59	52	20.7	9	63.4	54.8	5.4	—	23.7
1940–41 (treated cases):								
10–19	29	15.8	4	3.5	0	2.6	78.6	13.2
20–29	93	17.8	4	3.2	0	3.1	61.2	12.4
30–39	121	17.3	16	4.1	3.3	3.0	61.2	13.2
40–49	99	18.1	18	10.9	5.3	4.3	51.2	16.0
50–59	67	17.6	17	20.9	13.1	4.6	43.4	18.7
1945–46 (treated cases)								
10–19	31	16.7	0	0	0	2.7	58.1	13.1
20–29	40	15.3	3	5.0	5.0	5.1	42.1	16.2
30–39	63	11.0	6	12.7	6.8	5.2	35.2	17.7
40–49	95	14.7	9	10.5	5.6	5.7	35.7	19.2
50–59	73	13.1	8	21.9	12.3	6.4	34.5	18.7

*Corrected by exclusion of patients who died within twenty-four hours of admission.
†Among patients who recovered.

TABLE 4. *Influence of Sex and Race.*

SEX	RACE	No. of Patients	Mean Age	Alcoholic Patients	Case Mortality	
					TOTAL	CORRECTED*
			yr.		%	%
1936–37:						
M	White	86	36.4	10	29.1	22.8
M	Non-white	93	35.5	3	30.1	20.7
F	White	39	36.0	0	25.6	21.6
F	Non-white	43	35.5	0	39.6	31.6
1940–41 (treated cases):						
M	White	123	38.4	17	14.6	10.3
M	Non-white	162	36.9	4	6.2	1.9
F	White	62	37.6	1	3.2	1.6
F	Non-white	62	33.2	1	4.8	3.3
1945–46 (treated cases):						
M	White	96	45.6	15	25.0	11.1
M	Non-white	123	38.2	3	7.3	5.8
F	White	26	38.5	0	7.7	4.0
F	Non-white	61	34.0	0	3.3	3.3

*Corrected by exclusion of patients who died within twenty-four hours of admission.

being less than 0.0001, from those of 1940–41 in two respects: the decrease in white-cell count and the increased duration of fever after application of specific therapy. A possible explanation for these changes is that an increased prevalence of non-bacterial pneumonias during the war years had resulted in the erroneous inclusion of a considerable number of viroid pneumonias in the group with diagnoses of lobar pneumonia. Another possibility is that a change in the character of pneumococcal lobar pneumonia had occurred.

Influence of Age

As pointed out above the mean age of patients with lobar pneumonia increased from 1936–37 to 1945–46 (Table 2). Table 3 emphasizes this change and indicates that the apparent increase in mortality in the last year was due to the changing age distribution of the patients with lobar pneumonia. It will be noted that in 1936–37 the group of patients from thirty to thirty-nine years of age was the largest, with almost equal numbers in the younger and older groups; in 1940–41 there was a slight increase in the older age groups, but in 1945–46 there was a marked increase, the groups of patients between forty and forty-nine and fifty and fifty-nine each being larger than any of the younger groups.

Analysis by age groups demonstrates the same sharp increase in seriousness of lobar pneumonia with age that was noted in older reports before the introduction of chemotherapy.[1] The use of sulfonamides resulted in a sharp reduction of mortality in all age groups; the case mortality above the age of fifty, however, remained high. Although the rate remained essentially constant by age groups from 1940–41 to 1945–46 in the latter year, in all age groups except the few patients from ten to nineteen years old, the white-cell count was decidedly lower, and the therapeutic response as measured by critical decline of temperature was considerably less satisfactory (Table 3).

The duration of illness, type of medical care, degree of fever and x-ray findings did not vary consistently with age. The frequency of positive blood cultures was greater in the older age groups.

Influence of Sex and Race

Case mortality rates in 1936–37 showed no remarkable difference between males and females or whites and Negroes (Table 4). Similar observations have been the rule in the past.[1] In the patients receiving specific therapy in 1940–41 and 1945–46, the reduction in case mortality appeared equally striking among white females and Negroes of both sexes, whereas the rate among white males showed a considerably less satisfactory decline. The significantly higher average age of the white males in 1945–46 may have accounted for the high mortality in that year, but the average age of this group in 1940–41 was not markedly higher than that of the other groups. The greater frequency of alcoholism among white males may have been important, although it did not cause a greater mortality in 1936–37.

In both sexes and both races, the decrease in white-cell count and prolongation of fever mentioned above were noted in the 1945–46 group, even though the case mortality was little higher

Table 5. *Relation of Admission White-Cell Count to Response in Patients with Lobar Pneumonia.*

Year	White-Cell Count	No. of Patients	Case Mortality		Patients Afebrile in Forty-Eight Hours†
			total	corrected*	
	×10³		%	%	%
July 1, 1936, to June 30, 1937:					
	under 5.0	4	50.0	50.0	—
	5–9	24	16.7	4.8	—
	10–14	42	31.0	29.3	—
	15–19	50	12.0	12.0	—
	20–29	62	12.9	10.0	—
	over 29	36	41.7	34.4	—
July 1, 1940, to June 30, 1941 (treated cases):					
	under 5.0	5	20.0	0	75.0
	5–9	55	9.1	5.7	61.2
	10–14	76	7.9	2.8	57.2
	15–19	112	4.5	4.5	55.2
	20–29	108	4.8	4.8	56.6
	over 29	31	3.3	3.3	58.6
July 1, 1945, to June 30, 1946 (treated cases):					
	under 5.0	9	44.5	16.7	40.0
	5–9	73	9.6	4.3	40.6
	10–14	70	5.7	4.4	37.5
	15–19	55	14.5	13.0	38.3
	20–29	45	6.7	4.5	29.3
	over 29	9	11.1	11.1	25.0

*Corrected by exclusion of patients dying within twenty-four hours of admission.
†Among patients who recovered.

than in 1940–41. No consistent sexual or racial differences were noted in duration of illness before hospitalization, character of prior medical care, degree of fever or bacteriologic or x-ray studies.

Significance of White-Cell Count

Analysis indicates that the initial white-cell count was not correlated with response to therapy (Table 5). Patients with counts below 5000 showed an extremely high mortality, but the number of such cases was small. With this exception there seemed no constant tendency in any year for the response to therapy to vary with the white-cell count.

In 1936–37 only 12.8 per cent of patients had counts below 10,000, and 45.0 per cent had counts of 20,000 and above; in 1940–41, 15.3 per cent had counts below 10,000 and 36.0 per cent counts of 20,000 and more, whereas in 1945–46 the corresponding percentages were 31.4 and 20.7. During the decade there have been no changes in organization, procedure, or laboratory personnel that might have been responsible for the changes reported in white-cell counts. A study of the duration of illness prior to admission and of the possible effect of specific therapy prior to hospitalization has been made. These factors do not appear to have been significant (Table 6 and 7), nor did the influence of sulfonamide or penicillin therapy after admission to the hospital appear to have been contributory.

The possibility has been mentioned that the decline in white-cell count, as well as the retarded response to specific therapy, was due to inclusion in the group in which many cases of viroid pneumonias were studied. This possibility is not substantiated by the data in Table 8. The cases with white-cell counts between 5000 and 10,000 would be most likely to include such viroid pneumonias, but this group exhibited the same case mortality and showed a more rapid decline of fever than the patients with moderate or with marked leukocytosis.

The degree of leukocytosis showed no consistent relation with age, sex, race or bacteriologic or x-ray findings.

Bacteriologic Examination

Sputum cultures were obtained in 67.4 per cent of the lobar pneumonias in 1936–37, in 78.6 per cent in 1940–41 and in 71.6 per cent in 1946–47. In the first of these years, pneumococci were demonstrated either in pure culture or with other organisms in 90.9 per cent, in 1940–41, in 93.2 per cent, and in 1945–46, in 92.4 per cent. The pneumococci isolated from sputum showed considerable variation: in 1936–37, Type I, 16.0 per cent, Type II, 10.6 per cent, Type III, 8.9 per cent, Type IV, 1.2 per cent, Type VIII, 1.8 per cent and Type X and higher, 61.5 per cent; and in 1940–41, Type I, 18.9 per cent, Type II, 4.6 per cent, Type III, 13.1 per cent, Type IV, 8.9 per cent, Type V, 3.7 per cent, Type VII, 8.5 per cent, Type VIII, 10.0 per cent. Type IX, 2.7 per cent and Type X and higher, 29.6 per cent. In 1945–46, as noted above, typing of sputum cultures was not done.

Satisfactory blood cultures were obtained in approximately 65 per cent of patients with lobar pneumonia in each of the years under study (Table 8). The percentage of blood cultures reported positive was 20.5 in 1936–37, 20.6 in 1940–41 and 13.2 in 1945–46. In each year the mean white-cell count on admission of patients shown to have pneumococcemia paralleled that of the entire group (Table 8). The case mortality in patients with positive blood cultures was significantly higher than that in other patients. Study of a small group of patients having bronchopneumonia with blood cultures positive for pneumococci revealed white-cell counts and case mortality rates similar to those described above.

Table 6. *Influence of Therapy before Admission.*

Previous Therapy	No. of Patients	Mean Duration of Illness	Mean White-Cell Count	Case Mortality*
		days	*×10³*	%
1936–37:				
None	222	4.1	20.4	22.9
Sulfonamides	—	—	—	—
Penicillin	—	—	—	—
Other medication	39	5.8	20.3	20.6
1940–41:				
None	352	3.5	17.5	4.5
Sulfonamides	11	5.8	18.3	0
Penicillin	—	—	—	—
Other medication	66	4.1	17.9	11.1
1945–46:				
None	217	4.5	14.4	5.4
Sulfonamides	29	6.2	11.4	6.1
Penicillin	4			
Other medication	62	4.0	13.8	5.2

*Corrected by exclusion of patients who died within twenty-four hours.

The type distribution of pneumococci isolated from the blood in 1936–37 and 1940–41 paralleled that observed in the sputum. In 1945–46 Type II was most often isolated; this may have been the result of the well known high invasiveness of this type, and need not reflect a high incidence of Type II among all pneumonias in this year. It is noteworthy that a positive blood culture was obtained in only 1 of the 44 patients who had received specific therapy, which in most cases was inadequate, before admission.

In the patients with pneumococcemia who recovered, the duration of fever was considerably greater than that among patients with other lobar pneumonias. Again, the duration was longer in 1945–46 — 8.2 days — than in 1940–41 — 6.9 days.

The observation that even among patients with positive blood cultures the white-cell count was much lower and the decline in fever less rapid in 1945–46 than in 1940–41 serves further to eliminate the possibility that these phenomena observed in the entire group of lobar pneumonia were due to erroneous inclusion of viroid pneumonias in the latter group.

TABLE 7. *Duration of Illness before Hospitalization in Patients with Lobar Pneumonia.*

Duration of Illness before Admission	No. of Patients	Case Mortality	
		total	corrected*
days		%	%
1936–37:			
1	32	31.3	29.1
2	33	27.3	17.2
3	39	15.4	10.8
4	58	25.9	17.3
5	33	39.4	31.0
6	15	33.3	33.3
7 and over	43	41.8	34.2
Not stated	8	50.0	20.0
1940–41:			
1	81	4.9	2.5
2	75	4.0	2.7
3	93	7.5	3.4
4	56	8.9	3.8
5	41	4.9	0
6	16	0	0
7 and over	51	27.4	17.8
Not stated	16	50.0	33.3
1945–46:			
1	54	7.4	5.7
2	42	11.9	7.5
3	52	9.6	2.1
4	42	4.8	2.4
5	26	15.4	4.4
6	11	0	0
7 and over	67	17.9	11.3
Not stated	18	33.3	20.0

*Corrected by exclusion of patients who died within twenty-four hours of admission.

Medical Care and Duration of Illness Prior to Hospitalization

The possibility was considered that the characteristics of pneumonia were modified by the widespread use in recent years of sulfonamides and of penicillin by practitioners treating the patients before admission.

The data presented in Table 6 indicate that only a minority of patients with lobar pneumonia admitted to the Philadelphia General Hospital received medication prior to admission. A history of sulfonamide therapy was obtained in only 11 cases in 1940–41 and in 29 in 1945–46. An additional 4 patients in the latter year received penicillin. Presumably because of this therapy, the patients in this group were ill longer before hospitalization. In other respects, this group did not differ notably from patients not receiving specific therapy before admission.

The mean duration of illness before admission in each year was less in patients who recovered than in those who died. Table 7 indicates that in 1940–41 and 1945–46 this difference was accounted for chiefly by the high death rate among patients who gave a history of illness of a week or more before hospitalization. Surprisingly, there was no increase in mortality with increasing duration of illness prior to admission, provided that this duration was less than a week.

X-ray Examination

X-ray examination was made in 36.0 per cent of patients with lobar pneumonia in 1936–37, 43.6 per cent in 1940–41 and 85.2 per cent in 1945–46. In many cases the examinations were made in convalescence rather than on admission. Approximately half the examinations were reported to show consolidations typical of lobar pneumonia; the remainder, in most cases, disclosed resolving pneumonia. In slightly less than 5 per cent of cases, a diagnosis of lobar pneumonia was made despite x-ray reports of "patchy" or lobular pneumonia.

Complications

The frequency of septic complications fell from 7.3 per cent in 1936–37 to about 4 per cent in the years in which specific therapy was used (Table 9). Invasive pneumococci were apparently as prevalent in the lobar pneumonias of 1945–46 as in those of 1940–41, and it is noteworthy that patients with septic complications did not exhibit the low admission white-cell counts encountered in other patients. In all three years the case mortality in patients with septic complications was very high. Chronic alcoholism, presumably marked, was noted as a complication in 5 per cent of patients in each year. The group consisted predominantly of older white men. Curiously, the alcoholic patients showed no excess mortality in 1936–37 (Table 9), but in 1940–41 and 1945–46 the case mortality was proportionately many times that of the group as a whole. Severe alcoholism is seemingly a major factor in failures of specific therapy in pneumonia.

Discussion

The case mortality of lobar pneumonia observed at the Philadelphia General Hospital fell sharply after the introduction of sulfonamides, but no further

reduction occurred after penicillin was made available. The gross mortality appeared to rise slightly in 1945–46 as compared to that in 1940–41, but this was due to the greater proportion of older patients in the more recent year. The declining proportion of young persons is indicative of a lesser incidence or severity of pneumonia among younger patients in recent years.

Two highly significant differences were noted between the patients with lobar pneumonia in 1940–41 and those in 1945–46 — a further marked decline in degree of leukocytosis on admission, and a retarded temperature response to specific therapy. These characteristics are those of viroid pneumonias, and it seemed possible that the explanation lay in the inclusion in the series by erroneous diagnosis of a considerable number of viroid cases. Detailed analysis indicates, however, that this hypothesis is not tenable. Thus, the same characteristics were exhibited in pneumonias proved to be of bacterial etiology by demonstration of pneumococcemia, and patients with marked leukocytosis showed the same retarded response as those with normal white-cell counts. It appears that the pneumococcal lobar pneumonias of 1945–46 altered in certain respects from the lobar pneumonias of 1940–41 and earlier. The loss of the characteristic marked leukocytosis and dramatic response to sulfonamides or penicillin deprives us of two criteria that formerly seemed most valuable in the differentiation of bacterial and viroid pneumonias. A recent study by Racker, Rose and Tumen[4] has similarly demonstrated the inadequacy of these criteria, and roentgenologic criteria as well, for the differentiation of these two varieties of pneumonia.

The most plausible explanation for this increasingly ill defined line of demarcation between viroid and bacterial pneumonias may rest in the hypothesis suggested in 1944 by Francis[5] that the picture seen in atypical pneumonia represents the underlying process of most bacterial pneumonias, with the superimposed bacterial infection merely modifying to greater or less degree the basic nonbacterial disease. Such an interpretation obtains support from Hodges and MacLeod's[6] studies on pneumococcal pneumonia in the Army, in which epidemic surges of viral infection and epidemic outbreaks of pneumococcal pneumonia were closely associated. The increasing difficulty in differentiating bacterial and viroid respiratory infections, which is now generally experienced in clinical practice and which Ziegler and his co-workers[7] have documented, may thus be interpreted as being the result of a recent change in the relative intensity of the underlying viral and superimposed bacterial infections. The changes observed in lobar pneumonia at Philadelphia General Hospital during the past decade are explicable on the hypothesis that lobar pneumonias represent a heterogeneous group that in recent years has included a larger number of patients in whose disease the bacterial factor was relatively slight.

It is noteworthy that early reports on the use of sulfonamides, as well as of specific serum therapy, emphasized the necessity for early institution of

TABLE 8. *Patients with Pneumococcemia in Addition to Lobar Pneumonia.*

YEAR	NO. OF PATIENTS	TYPE OF PNEUMOCOCCUS					MEAN WHITE-CELL COUNT ON ADMISSION	CASE MORTALITY		MEAN DURATION OF FEVER†
		I	II	III	IV	V AND HIGHER		TOTAL	CORRECTED*	
							x10³	%	%	days
1936–37	33	7	3	2	0	22	20.0	45.5	42.0	9.9
1940–41	59	18	3	4	9	25	18.9	25.4	21.4	6.9
1945–46	26	4	12	0	1	7	13.0	42.3	21.1	8.2

*Corrected by exclusion of patients who died within twenty-four hours of admission.
†Among patients who recovered.

TABLE 9. *Influence of Complications on Case Mortality.*

YEAR	TOTAL PATIENTS	TOTAL TREATED PATIENTS	PATIENTS WITH EMPYEMA	PATIENTS WITH MENINGITIS	PATIENTS WITH ENDOCARDITIS	PATIENTS WITH PERICARDITIS	TOTAL SEPTIC COMPLICATIONS*	MEAN WHITE-CELL COUNT	CASE MORTALITY		ALCOHOLIC PATIENTS	CASE MORTALITY OF ALCOHOLIC PATIENTS	
									TOTAL	CORRECTED†		TOTAL	CORRECTED†
								x10³	%	%		%	%
1936–37	261	—	12 (4.6%)	2 (0.8%)	2 (0.8%)	4 (1.5%)	19 (7.3%)	19.8	52.6	35.7	13 (5.0%)	30.8	25.0
1940–41	—	409	8 (2.0%)	2 (0.5%)	4 (1.0%)	1 (0.2%)	15 (3.7%)	21.4	46.6	33.3	21 (5.1%)	38.2	27.8
1945–46	—	302	8 (2.7%)	3 (1.0%)	2 (0.7%)	2 (0.7%)	13 (4.3%)	18.1	53.8	45.4	16 (5.3%)	31.3	21.4

*Excluding duplications.
†Corrected by exclusion of patients dying within twenty-four hours of admission.

treatment, whereas the lack of correlation between duration of illness before application of therapy and the case mortality observed in this study is suggestive of a diminishing importance of the bacterial factor.

The case mortality rates of lobar pneumonia reported in England and in parts of western Europe prior to the introduction of sulfonamides were considerably lower than the high rates experienced in this country before specific drug or serum therapy was used.[1, 8] This may indicate that pneumococcal lobar pneumonia was not in the past a homogeneous entity and that the viral factor or the bacterial factor, or both, varied geographically.

The diminishing importance of the bacterial factor need not be attributed to the influence of sulfonamides and of penicillin. The mortality from lobar pneumonia had declined sharply between 1925 and 1937, to a far greater degree than could have been due to the limited use of serum therapy.[1] As in tuberculosis the decline in pneumonia cannot be explained wholly by the therapeutic advances that have been made, and probably the changes in both diseases are due not to modification of the virulence of bacteria, but to constitutional and environmental factors affecting host resistance.

The marked increase in case mortality with age deserves emphasis, for special attention to this factor is required in any evaluation of therapeutic trials in pneumonia. The strikingly low case mortality (less than 1 per cent in lobar pneumonia reported in the Army[9] and the Navy[10]), during the war years is not likely to be duplicated in the general population.

The high rates among patients over the age of fifty noted in recent reports from the Cook County Hospital[11] and the Gallinger Hospital,[12] as well as in the present study, and the high rates still observed in patients with alcoholism, empyema, meningitis, endocarditis and pericarditis indicate that the therapeutic problems of pneumonia are not completely solved.

Summary

A study has been made of lobar pneumonia at the Philadelphia General Hospital in 1936–37, a year in which specific therapy was not employed, in 1940–41, a year in which sulfonamides were generally applied, and in 1945–46, a year in which penicillin was available as an adjuvant to the sulfonamides. The case mortality rates were 23.3 per cent, 5.4 per cent and 6.5 per cent for the three years, the apparent slight increase in the last year being due to a striking rise in age of the patients.

Although the mortality of lobar pneumonia did not vary significantly between 1940–41 and 1945–46, highly significant differences between these years were observed in two respects: a reduction in white-cell counts on admission and a retarded temperature response to specific therapy. Detailed analysis indicates that these changes cannot be attributed to erroneous inclusion in the 1945–46 series of large numbers of viroid pneumonias.

It is concluded that pneumococcal lobar pneumonia as observed in 1945–46 had altered significantly from the disease encountered in previous years, and in such fashion that it was clinically difficult to distinguish from viroid pneumonias. It is suggested that lobar pneumonia is not, and has not been, a homogeneous entity but represents rather an underlying viral process modified to greater or less degree by superimposed bacterial infection. The relative importance of the viral and bacterial factors in lobar pneumonia appears to have altered in recent years.

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PRINCIPLES OF THE MASSACHUSETTS MEDICAL SOCIETY*

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THE concept of this symposium came from the late Dr. Michael A. Tighe. He believed that it was time we told each other and the people of the Commonwealth where we are now and where and how we are going.

The following are the principles of the Massachusetts Medical Society as developed by the Subcommittee on Medical Economics and adopted by the Council about a year and a half ago:

> The objective of adequate medical care in our free society is to make available to everyone — regardless of race, color, creed, financial status or place of residence — every known essential preventive, diagnostic and curative medical service of high quality. The attainment of such medical care must necessarily be an evolutionary process which will require the co-operation of all concerned over a period of years.
>
> The success of any plan for medical care is dependent on the mutual co-operation of the public, those rendering professional services and the administrative agencies. This co-operation can be obtained only if those rendering the services are convinced that they will have a continuing authoritative voice in the formulation and execution of policies and plans, thereby assuming their proper share of responsibility.
>
> Provision of adequate medical care for those unable to obtain it by voluntary prepayment plans or by direct payment is the responsibility of the local or state government. Part of the burden of this responsibility may be assumed by charitable agencies. Federal grant-in-aid to state programs administered by state boards of health is an acceptable method of helping to meet this responsibility.
>
> The medical care of those who are able to purchase it by voluntary prepayment plans or by direct payment is the responsibility of the individual.
>
> Eligibility for receiving benefits under a program aided by federal grants should be determined by the individual states.
>
> The patient shall have free choice of his physician, group of physicians, clinic or hospital from among those participating in any plan, provided that the physician, group of physicians, clinic or hospital shall have the right to refuse or to accept the patient.
>
> Physicians and other qualified persons rendering medical care shall receive adequate remuneration for their services.
>
> The physician shall be free to elect or reject without prejudice participation in a medical-care plan. The rights of the physician as to the choice of methods by which he is to be paid shall be fully protected.
>
> The Massachusetts Medical Society looks upon these basic principles as essential to the development of any successful medical-care plan and, as guides by which to evaluate medical-care plans that may be proposed in the future, with the understanding that changing conditions may require their later revision.

I remember a number of years ago when we, in the Committee of Public Relations, under the able leadership of Dr. Ernest L. Hunt, made some spot studies in adequacy of medical care in this state. I remember in that same committee when Dr. Nathaniel W. Faxon discussed prepayment hospitalization; he stated that such a plan would not be started without our approval and would proceed only with our approval. I remember that in that same committee discussion of medical-care plans later developed and that, under the brilliant and aggressive leadership of Dr. James C. McCann, the Blue Shield was conceived and launched. At about the same time the White Cross was born. This was an experiment in medical care sponsored by men who were impatient with such "inadequate" concepts for solution of problems in medical-care distribution as the Blue Shield then seemed to them. I have always thought that these men could have performed a service by reporting on the causes of failure factually and objectively.

You will hear today where Blue Cross and Blue Shield stand *now*. I think that Massachusetts can be proud of its progress in trying to satisfy unmet needs in medical-care distribution. Social changes properly proceed slowly and safely, not at a speed that would satisfy the impatient reformers who blueprint Wagner–Murray–Dingell bills, but fast enough to arouse protests from the ultraconservatives.

The next five years, the next one or two years and perhaps the next few months will be critical. Change is needed, and with a properly statesmanlike attitude we can provide leadership that will continue to earn us the respect and confidence of a people who have a right to expect leadership from us because we are specialists in the field.

Let us consider casually some of the factors that must be borne in mind as we proceed toward adequate medical care for all the people.

* * *

When we consider adequacy of medical care for all regardless of economic status, we must recognize that there is more involved than rhetoric. Cost is not the chief barrier to utilization of available medical care. For years the Commonwealth has had cancer clinics accessible to all the people that make it entirely unnecessary for anyone to be host for long to unrecognized cancer. People still have symptoms for an average of about four months before they seek medical care. There is a great deal in the field of preventive medicine — for example, in tuberculosis and venereal disease — that could be practically eliminated if people would use the facilities for diagnosis and care that are now available. Progress is being made all the time, of course, and the Massachusetts Medical Society is continually doing a great deal toward helping to get medical care of a better quality to the consumer.

*Presented at the annual meeting of the Massachusetts Medical Society, Boston, May 20, 1947.

†Formerly, president of the Massachusetts Medical Society.

I am very sure that if there were more and better district health councils throughout the Commonwealth tremendous strides would result. The district health council is an organization consisting of representatives of all the facilities and agencies concerned in the distribution of medical care, such as the doctors, the hospitals, the nurses, the druggists, the dentists, the public-health administrators and the social workers. These organizations could analyze the available facilities and see that there is more adequate utilization of those existing, and also supplement these by assisting in the development of services that are deficient.

There is a great need for more utilization of dentists. In England, where government insurance has been in effect for many years, of the 14,000,000 people eligible for dental care, only 7 per cent avail themselves of the service. Massachusetts is still one of the states whose populations have the poorest teeth in the country in spite of a relatively low cost barrier. Very recently Navy medical officers conducted studies of housing, sanitation and health of our coal miners and found conditions that were not satisfactory. These people need better facilities but particularly more education in living standards. Deficiencies even in such fundamentals as running water and indoor toilets exist to a surprising degree. The metropolitan health survey found very recently that there were 100,000 people living in Washington, D. C., without these facilities.

Some planners who sit in ivory towers think that all medical care should be dispensed by groups. There are plenty of good reasons why more group practice should be carried on, but that will develop better by evolution — through trial and error. Groups were more popular for a while after World War I, but there were many failures and only a few brilliant successes. Time does not permit analysis of the causes of failure. The general practitioner is the backbone of the system of distribution of medical care to the people, and I hope that he always will be. I am willing to debate this with anyone who does not agree. The general practitioner is as essential to medicine as the infantryman is to the army. Every general practitioner has his own informally organized group. He knows who among those available is the best qualified for the patients who need a specialist. It is only relatively few who need specialized diagnostic care or treatment. It is not good economy to consult the specialist for everything. There is a degree of obligation in organized groups to utilize only group personnel. This limits choice too much in some cases.

There are a group of people — the medical indigents — who are able to meet the expenses of ordinary medical care but once in a few years are confronted by unusual diagnostic costs and perhaps surgery and hospitalization. These people vary in number with the degree of prosperity in the country. But they are enough of a problem so that it seems probable that ultimately the only logical way to meet the cost is by governmental subsidy. Many of those who would have been medically indigent have been lifted out of that group by being able to pay for medical care through Blue Cross and Blue Shield. I have patients who were formerly unable to pay for obstetric care and are now proud that they can meet these costs in this way. I have figures that indicate that in a one-hundred bed hospital the doctors on the ward services contribute more than $100,000 a year in medical and surgical services to the community. We have done very little complaining about this. Many people think that we are paid a salary for these services.

The Taft Bill (S. 545) proposes to have the federal Government subsidize the state to take over this burden. It would be essential to have a continuing authoritative voice given to the doctors in the management of the professional side of such a plan. In England, under a new plan, the Labor Government has taken over medicine and the hospitals lock, stock and barrel. The importance of proper technical advice from the doctors has not been realized. There is an advisory board, but it has been given no power; one of the medical statesmen of England recently said, "You know that kind of a board can cut no ice." The Massachusetts Department of Public Health appreciates the necessity of cooperation with technical advisory boards. The Department of Public Welfare is beginning to learn. Federal financing means that the federal Government will need to raise the money; federal money comes from the taxpayers, and Massachusetts pays a good share of federal taxes. We approve of the principle of taxing Massachusetts more to provide for some of the poorer states — in the same way that we who are better able to bear the tax burden take care of the poor in our own town.

The physician should receive adequate remuneration for his services. The cost to the medical schools for education is about $2400 per year per student. One New England school a few years ago had $5000 in the budget per medical student per year. Dr. Elliott P. Joslin states that the average doctor in the Commonwealth practices only fifteen years. The man or woman who goes to college for four years and to medical school for four years has to spend at least $10,000 of somebody's money for his education. Then he has from two to five years' training in a hospital before he begins to pay off the mortgage. He has barely time to get a proper basis for living for his family and enough insurance to keep them from becoming public charges before his years of usefulness are waning. Certainly, those who know the facts do not expect the doctor to do the job he does for less money.

The Massachusetts Medical Society has a few leaders who have constantly tried to discover and meet the medical needs of the Commonwealth and

of the country. As we come into these times of more active social adjustment we have made very considerable strides in better organizing ourselves to serve the people. We might have done a good deal more in the past, but too many of us have been too busy meeting the needs on the firing line; moreover, social changes develop along sounder lines if the whole body politic has a chance to get conditioned to change at an evolutionary rate. It is axiomatic that the best that is known is ahead of the best that is done in this as in all fields.

281 Main Street

WHO CARES FOR THE EPILEPTIC?*

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EPILEPSY is a larger public-health problem than is generally realized, even by doctors. Its supposed infrequence is due to the practice of concealment and to the widespread popular belief that for epilepsy there is no effective treatment. The United States Selective Service figures of 1917 gave for Massachusetts an incidence of 0.59 per cent (as compared with 0.515 for the whole country). Yet medical officers know that thousands of epileptic patients were not detected by the Selective Service examinations; thousands risked a lie to risk a life for their country (and the esteem of their fellows). If the statistics are accepted, epilepsy is as common as active tuberculosis, diabetes or crippling infantile paralysis.

In Massachusetts, how many epileptic patients are supervised medically? How many are cared for in clinics, and how many in private offices? How is the burden distributed among practitioners and the various specialists? Do physicians wish for additional information about epilepsy and newer methods of therapy? In the summer of 1946 the Committee on Public Health of the Massachusetts Medical Society, which is commissioned by the Society to "foster the knowledge of disease by any appropriate measures," sent a letter to each member of the Society asking for information that would help to answer these questions. The American Epilepsy League inspired the effort. Expenses were met by the Bay State Society for the Crippled and Handicapped, which helps to support the Seizure Unit of the Children's Hospital of Boston. Letters went to 5539 physicians. Of these, 2997, or 54 per cent, replied to either the first or a follow-up letter. Deducting 201 replies from men who were in, or just out of, service, 2796 blanks remained.

Patient Load

The questionnaire asked for the number of epileptic patients who had been seen privately or in clinic during the previous twelve months. Of the physicians replying, 1613, or 58 per cent, had "seen" epileptic patients in the past year, and 1183, or 42 per cent, had not. Of the 1613 doctors who treated these patients, 1472, or 91 per cent, did so in private offices, and 316, or 19 per cent, in a clinic. Ten per cent saw patients in both places.

Doctors were asked the approximate number of epileptic patients seen in the year: 11,434 patients were reported, of whom 60 per cent were office and 40 per cent were clinic cases. This does not include 2746 patients cared for in institutions. The numbers are exaggerated because a given patient may have visited more than one physician or may have been seen both as a clinic and as a private patient.

Distribution of Patient Load

The 1472 doctors who reported office treatment of epileptic patients during the year saw a total of 6905 patients, or an average of 4.7 each. The much smaller number of doctors, 316, saw a total of 4529 patients in a clinic — an average of 14.3 per doctor. If the total number of noninstitutional ("extramural") patients are divided equally among the doctors who treated patients, the number per doctor is 7.1, of which 4.3 are office and 2.8 clinic cases. If the 11,434 patients are divided among the 2796 "active" doctors answering the questionnaire, the distribution is 2.5 office and 1.6 clinic, with a total of 4.1 patients. Probably each physician who returned the questionnaire treated more epileptic patients than those who consigned it to the wastebasket. Assuming that the 46 per cent of doctors who did not return the questionnaire saw only half as many of these patients as those who did, the stated number of epileptic patients, on the basis of equal distribution among the 5338 physicians, provides each with three patients. This number is undoubtedly too high because of duplication. Patients reported by the heads of x-ray departments and other laboratories were eliminated because they would have been reported also by the referring physician, but other duplications could not be detected without a request for the names of patients. The incidence of epilepsy among men examined for

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the Army in 1917 would give Massachusetts approximately 20,000 epileptic patients, or something like 4 patients to each doctor. Probably not more than half this number were seen by the doctors in Massachusetts during the year in question. This conclusion will not surprise those who examined Selective Service registrants in the last war. Many acknowledged patients had not consulted a physician, believing that doctors could offer no effective treatment.

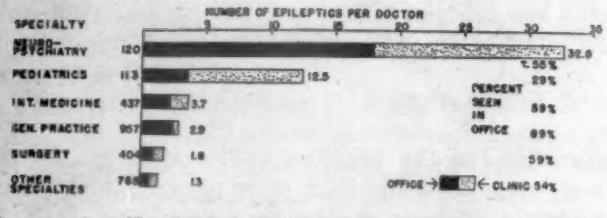

FIGURE 1. *Number of Epileptic Patients Seen for Each Doctor Answering the Questionnaire.*

Neuropsychiatry includes neurosurgery. The figures at the left refer to the number of doctors. The solid portions of columns refer to office, and the dotted portions to clinic patients. The percentage figures at the right give the proportion of all patients seen in the office.

Patient Load and the Specialties

Physicians were asked to name their specialty. The number of patients treated annually by practitioners and various specialists is shown in Figure 1. As would be expected, the group of neurologists, psychiatrists and neurosurgeons heads the list, with an average of 32.8 patients per doctor (the five neurosurgeons who reported had an average load of 68 patients). Next in importance are the pediatricians, who saw an average of 12.5 epileptic patients. Aside from these two groups — numbering only 233 doctors — the internists, general practitioners, surgeons and other specialists saw, respectively, from 3.7 to 1.3 such patients in the year.

In view of the present agitation for lower cost of group treatment of patients, comparison of the numbers of patients treated as private and as clinic patients deserves special attention. Of the six groups presented in Figure 1, all but two saw a little more than half of the epileptic patients privately (from 54 to 59 per cent). The two groups that were far outside this zone were the general practitioners, with 89 per cent office patients, and the pediatricians, with only 29 per cent of patients seen in the office and 71 per cent seen in clinics. Since clinic work carries little or no monetary reward, pediatricians must be carrying a disproportionate share of the charity load. Whether this preference of the parents of the epileptic child for the clinic is due to economic conditions or to a belief as a result of publicity that better treatment can be obtained in the clinic is not clear from this survey. The survey of pediatric service now going forward should demonstrate whether other diseases of children tend to receive care in clinics at the expense of office practice.

The preceding data may give the impression that the care of epileptic patients is in the hands of neuropsychiatrists and pediatricians. Study of the share of each specialty in carrying the total patient load demonstrates the incorrectness of this view.

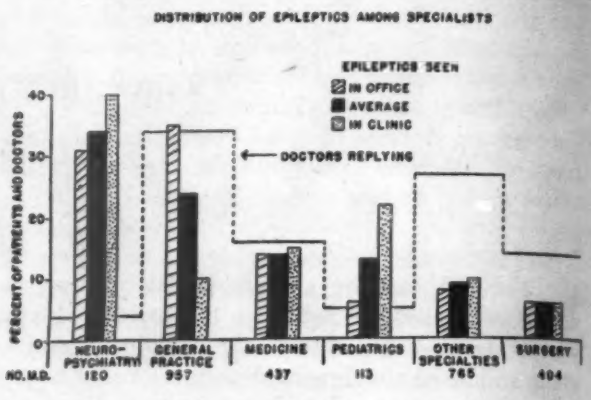

FIGURE 2. *Distribution of Epileptic Patients among Groups of Doctors.*

The columns represent the proportion of the total of 11,434 patients who were seen by the specified doctors. The horizontal lines give the proportion of the total of 2796 doctors who belong to each specialty. The hatched columns represent patients seen privately, and the dotted columns those seen in clinics.

TABLE 1. *Distribution of Office and Clinic Patients among Various Groups of Doctors.*

SPECIALTY	DOCTORS		PATIENTS SEEN IN OFFICE		PATIENTS SEEN IN CLINICS		ALL EPILEPTIC PATIENTS	
	NO.	PER-CENTAGE	NO.	PER-CENTAGE	NO.	PER-CENTAGE	NO.	PER-CENTAGE
Neuropsychiatry	120	4	2,148	31	1,797	40	3,945	34.5
General practice	957	34	2,454	35	311	7	2,765	24.2
Medicine	437	16	937	14	661	15	1,598	14.0
Pediatrics	113	5	412	6	1,000	22	1,412	12.3
Other specialties	765	27	533	8	469	10	1,002	8.8
Surgery	404	14	421	6	291	6	712	6.2
Totals	2,796		6,905		4,529		11,434	

Neuropsychiatrists, neurosurgeons and pediatricians treated only 37 per cent of office and 47 per cent of all patients. This is because these specialties constitute only 9 per cent of the doctors who responded to the questionnaire. The essential data are presented in Table 1. The columns of Figure 2 represent the distribution of extramural patients among the six groups of doctors, and the horizontal lines indicate the distribution of the doctors themselves. Thus, at the left of the figure, neuropsychiatrists number but 4 per cent of the number of doctors replying, but they saw 34.5 per cent of the 11,185 patients reported and, although each treated fewer clinic than office patients (Fig. 1), they saw a larger proportion of the total clinic cases than of the total office patients. The general practitioners carry the next largest load — namely, 35 per cent of office and 24 per cent of all patients. Practitioners and internists combined saw approximately half (49 per cent) of all office patients. The neuropsychiatrists and pediatricians combined saw 62 per cent of clinic patients. A comparison of the height of columns and of the solid line in Figure 2 displays the proportion of patients seen by various groups of doctors in relation to the numbers of doctors in these groups. Thus, neuropsychiatrists and pediatricians saw a large proportion of patients in relation to their own meager numbers. Surgeons, practitioners in clinics and other specialists saw relatively few epileptic patients. This tabulation, like that of Figure 1, emphasizes the relatively large clinic load carried by pediatricians. They receive relatively small recompense for the work of this nature that they do. As would be expected, various specialties such as the eye, ear, nose and throat, orthopedic and skin take care of relatively few patients with epilepsy.

Physician Interest in Newer Knowledge

The degree of mistreatment of a given patient is measured by how far the given therapy falls short of utilizing the best possible methods. On each accession of knowledge a previously "good" form of therapy becomes mistreatment, or at least inadequate. The same statement is as true of social as of drug therapy. For many centuries effective medical and surgical therapy was nil. Discoveries of the last ten or twelve years mean as much for the present-day epileptic person as the discovery of ether meant to the surgical patient a century ago. Yet, as neurologists of the Selective Service boards who questioned the raw mass of young men can testify, many patients with the Hippocratic disease either receive no care or treatment little better than that prescribed by Hippocrates himself. Massachusetts may be called the home of electroencephalography, of modern anticonvulsive therapy, or research and of interest in the disorder. Massachusetts has facilities for the care of epileptic patients unequaled elsewhere: the headquarters of the International League Against Epilepsy and of the American Epilepsy League, a dozen electroencephalograph laboratories, the Monson State Hospital, a national center for treatment and research at the Cushing Veterans Administration Hospital and special clinics for epilepsy in several hospitals. Unfortunately, facilities are too much concentrated in Boston. The New England Epilepsy League hopes to learn of physicians in New England who are both interested and competent in handling epileptic patients. The diagnostic, research and training center recently established at the Children's Hospital in Boston with the aid of the Bay State Society for the Crippled and Handicapped plans an extension of its services to physicians, hospitals and social agencies throughout the Commonwealth. Like charity, the application of medical knowledge does not always begin at home, and probably only a minority of the epileptic patients of Massachusetts are today receiving adequate medical and social care.

Social therapy is even more antiquated than medical. Twenty-six per cent of the colleges and universities of New England have a blanket rule against admission of scholastically qualified but epileptic students; the great and good Massachusetts General Hospital, birthplace of medical social service, will not engage a person who has a history of seizures, and the great Commonwealth of Massachusetts with a law that allows a handicapped worker to waive his rights to accident compensation will not extend that privilege to epileptic patients, nor will it permit the physician to give contraceptive advice to his epileptic patient who wants marriage but not children. Fourteen states of the Union forbid the epileptic person to marry, and the United States Government subjects the epileptic patient who comes to this country for medical advice to an embarrassing delay on Ellis Island.

To meet the need of doctors, social agencies and patients for up-to-date information about epilepsy and its medical and social therapy, the American Epilepsy League has assembled a series of medical reprints and popular articles, as well as several books. With the original questionnaire went a list of twelve of these articles and several books. Physicians were asked to check those desired. Of the 785 doctors who answered the first letter, 578, or 73 per cent, requested one or more reprints. The proportion was 80 per cent of the 434 doctors who saw patients, and 58 per cent of the 144 doctors who did not. These 578 doctors asked for three thousand, two hundred and thirty-three pieces of literature, or 5.6 per doctor. This average number was 5.9 for doctors who saw epileptic patients and 4.5 for those who did not. Of all articles requested, 73 per cent were technical, and 27 per cent popular — for the benefit of patients and their friends and relatives.

SUMMARY

Backed by the Committee on Public Health of the Massachusetts Medical Society and the Bay State Society for the Crippled and Handicapped, the American Epilepsy League sent questionnaires to all members of the Medical Society. Of 2796 doctors replying, 58 per cent had treated epileptic patients during the previous year. Of these, 91 per cent saw them in the office, 19 per cent in the clinic, and 10 per cent in both office and clinic. Of the 11,434 patients treated, 40 per cent were clinic and 60 per cent were office patients. Equally distributed, there would be 4.1 patients for each doctor who returned the questionnaire. Taking into account the duplication in this survey, probably not more than half the estimated 20,000 epileptic persons in Massachusetts are receiving active medical supervision.

Among all doctors replying, the average neuropsychiatrist or neurosurgeon saw 33 patients, the pediatrician 12, and other specialists and general practitioners from 3.7 to 1.7 each. Pediatricians treated 71 per cent of their epileptic patients in clinics, whereas all other doctors saw only 33 per cent there. Of all epileptic patients treated privately, the general practitioner saw the largest proportion — 35 per cent; 31 per cent were seen by neuropsychiatrists, and 14 per cent by internists. Of all clinic patients, 40 per cent were seen by neuropsychiatrists, 22 per cent by pediatricians and 15 per cent by internists. Pediatricians constituted only 5 per cent of the doctors who reported, but they treated 22 per cent of all clinic patients. They bear an unusually heavy load of charity patients. Of the 785 doctors who responded to the first questionnaire, 73 per cent requested reprints of articles on epilepsy, of which 73 per cent were technical in nature. Study of the questionnaires returned, together with our general experience, convinces us that both medical and social treatment of epileptic persons in Massachusetts and other states falls far short of utilizing knowledge gained during the past dozen years.

A STUDY OF VIRUS CARRIERS FROM A POLIOMYELITIS OUTBREAK AT A BOYS' CAMP*

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SMALL, localized outbreaks of poliomyelitis offer unusual opportunities for epidemiologic study. The more isolated the population unit under observation, the less complex appears the task of tracing chains of infection. However, it remains for future discoveries to determine how true this may actually be so far as poliomyelitis is concerned.

A recent outbreak of poliomyelitis in a boy-scout camp in western Massachusetts seemed to be particularly well suited for epidemiologic study. In the first place, prior to its occurrence, no cases of infantile paralysis had been reported from all of western Massachusetts for three months. Furthermore, the location of the camp near the summit of an isolated mountain reservation reduced the opportunity for outside contact of campers and personnel, although the camp cannot be described as a truly "isolated community."

Investigation of this outbreak was instituted after the rather sudden occurrence of 3 cases at the camp in July, 1946, when it was decided to disband the organization. Nearly all personnel returned home, with the exception of 20 persons who, for one reason or another, remained behind. Those events are presented graphically in Figure 1.

The plan of the study was to determine the carrier rate in the group of campers who were most heavily exposed to, or perhaps together with, known cases, as measured by virus isolations from throat and stool cultures.

It was believed that a number of features could be learned from this approach. Recent investigations have demonstrated that the poliomyelitis virus may be isolated more readily from stools than from material obtained from the oropharynx of patients[1]; however, observations on the relative frequency of intestinal as opposed to throat carriers among healthy contacts are few in number.[2, 3] It was proposed in this study to compare unpooled serial specimens (throat swabs and stools) obtained from contacts over a period of several weeks. Furthermore, since it is not known how often healthy carriers may directly transmit virus to others, investigation of children in households to which exposed campers

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returned also presented a limited opportunity to acquire new data on this point.

Material and Methods

The camp in western Massachusetts is referred to as Camp Pfd. Since all the clinical cases of poliomyelitis appeared in one of three groups of campers, it was decided to develop the laboratory investigation with this one group as the focal point. Because the camp had been dispersed at the time the study was begun, the aid of the local health department and visiting nurses* was sought in obtaining laboratory specimens. From the time of the outbreak, throat swabs and stool samples were obtained three times a week for four weeks from 18 of the 26 members of this group. Whenever possible, similar specimens were also taken from children in households to which exposed campers had returned. For serologic studies, each of the selected group of campers and their household contacts was subjected to three bleedings, one at the time of the initial visit and two others at intervals of three weeks. Blood, throat and stool specimens were also obtained from 7 other campers who were not members of the group in which the clinical cases occurred.

Throat swabs were placed in 1 cc. of water in a lusteroid tube and frozen immediately after being obtained. Stools were also frozen as soon as they were collected by the health-department personnel. The blood was centrifuged, usually on the day of collection (or within twenty-four hours during which it was kept in the icebox). Serum was drawn off and frozen.† All material was kept frozen, even during transport to New Haven, until it was prepared for animal inoculation or testing.

Virus testing. In general the methods followed have been described in previous communications from this laboratory.[1, 4, 5] Throat specimens were prepared for intracerebral inoculation by elution from the swabs and subsequent etherization.[6] Stools were also inoculated intracerebrally after their processing in the ultracentrifuge.[4] Rhesus (*Macaca mulatta*) monkeys were used as test animals — as a rule, one monkey being utilized for each test. All positive results for virus were confirmed by histologic findings of typical lesions in the spinal cords.

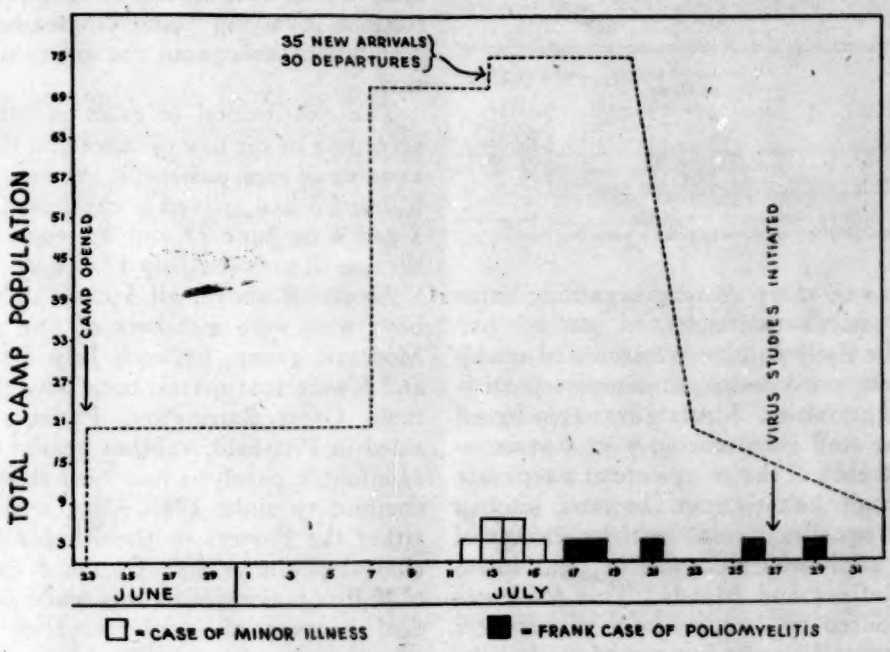

Figure 1. *Occurrence of Clinical Poliomyelitis at Camp Pfd in Relation to Camp Population.*

Neutralization tests. These were carried out with the Lansing and Y-SK murine-adapted, monkey-pathogenic strains of poliomyelitis virus. The technic was similar to that outlined by the Commission on Neurotropic Virus Diseases of the Army Epidemiological Board,[7] constant amounts of virus being used with varying dilutions of serum.

Epidemiology

The camp grounds covered an area of several acres and were located near the summit of a mountain (elevation, 1930 feet) in Berkshire County,

*Misses Ann M. Thompson, R.N., Charlotte Cornwell, R.N., Beaulah Zilling, R.N., and Justine Baldisserotto, R. N., helped in the collection of these specimens.

†We are indebted to Dr. Helen M. Scoville, House of Mercy Hospital, Pittsfield, for her aid in preparing the serum.

Massachusetts. Tents were placed in three areas, each about 50 yards in diameter and 100 yards from each other. Another section of the camp site was set aside for a screened kitchen cabin, unscreened mess and utility tents, an infirmary, several odd cabins and tents occupied by members of the staff. Swimming and water sports were carried on in a fresh-water lake several acres in extent, located below the level of the rest of the camp.

The personnel of the camp was divided generally into four groups, three of campers (Rangers, Pioneers and Blue Moccasins) and one staff group. The ages of the campers ranged from twelve to eighteen years. There was no sharp division regarding home town or date of arrival at camp.

TABLE 1. *Date of Arrival and Onset of Cases.*

CASE No.	DATE OF ARRIVAL AT CAMP	DATE OF ONSET
1	July 7	July 17
2	July 7	July 18
3	June 23	July 21
4	June 30	July 26
5	July 7	July 29

Sports and the daily routine were carried on by groups. However, on occasion all campers participated in general activities. Meals were eaten by all campers and the staff simultaneously in a common dining room, but each of the groups ate at a separate table. Although all the food from the camp kitchen was distributed equally among the three groups of campers, some additional food was brought in on Sundays by relatives and friends. This food was generally distributed by campers only to members of their own group. This was but one of the indications that in spite of the isolated location, the community was in close touch with the outside world.

The Ranger and Pioneer groups were housed in large tents, 8 campers being assigned to each tent. The leaders and counselors for each of these groups were in two-man tents. The campers and counselors of the Blue Moccasin group were housed in seventeen tents, each tent housing 2 persons. Sewage disposal was by pipe and pit urinals and by pit latrines covered with unscreened boxes. Garbage was carried away from the camp grounds and disposed of. The milk was pasteurized and of good quality, and arrived in 40-gallon cans. At mealtime the milk was poured into pitchers for individual tables. The food was obtained from recognized sources, and all perishable foods were kept on ice. The water supply came from a tubular well, and tests revealed it to be free from bacterial contamination.

The first group of about 20 persons, consisting of staff members, counselors and junior leaders, arrived in camp on June 23, 1946 (see Fig. 1). The first contingent of campers, comprising more than 50 boys arrived on July 7, when some of the first group returned home. A third group of approximately 35 campers arrived on July 13, when 30 of the original campers went home. With the exception of 20 persons, all personnel returned home between July 20 and 23.

According to the infirmary records, between July 12 and 16 there occurred 6 cases of minor illnesses in which the diagnosis was indefinite but the signs and symptoms were compatible with suspected (abortive) poliomyelitis. Although this diagnosis was not considered at the time, the patients were seen to be ill by the camp nurse. There were two small epidemics of diarrhea, primarily among the Pioneer group during the first two weeks of camp, and, in addition, a number of upper respiratory infections involving about 30 per cent of the camp population throughout the entire time of its operation.

The distribution of cases of infantile paralysis, according to the day of onset and the time of arrival at camp of each patient, is shown in Table 1. Cases 1, 2 and 5 had arrived in camp on July 7, and Cases 3 and 4 on June 23 and 30 respectively. They all became ill between July 17 and 29.

As stated above, all 5 cases occurred among 31 boys who were members of one group, the Blue Moccasin group, between July 7 and 14. Cases 1 and 5 were tent mates; both boys lived in the same town, Great Barrington. Patients 2, 3 and 4 resided in Pittsfield, another nearby town. No cases of infantile paralysis had been reported from either community since 1945. Not a single member of either the Pioneer or the Ranger group developed clinical poliomyelitis. Of the 5 cases, a diagnosis of bulbar poliomyelitis was made in 4. One patient died because of involvement of the respiratory center, and another received care in a respirator for a period of several months.

RESULTS OF LABORATORY INVESTIGATION

Establishment of the Strain of Virus and Attempt at Identification

The strain was first isolated readily from the pooled fecal specimens obtained from 3 of the hospitalized patients (Mo., He. and La.). Three serial passages of the virus in monkeys were carried out, and attempts were made with central-nervous-system material from each monkey passage, as well as with infective human stools, to adapt the virus to mice and cotton rats. Whereas the strain took easily in monkeys, no evidence of disease was seen in the rodents, even when such technics as concentration in the ultracentrifuge,[8] blind passage and Milzer's autolyzed brain method[9] were used.

Although the Pfd camp strain has not proved to be pathogenic for rodents, attempts were made to determine whether it was related immunologically to the Lansing and Y–SK strains. Convalescent and

hyperimmune monkey serums were prepared for the camp strain, and neither serum neutralized Lansing or the Y–SK strain.

Thus, the Pfd strain of virus appears to be typical of the usual type in the experimental disease produced in monkeys and in its failure to take in rodents. Moreover, no relation was demonstrated between this strain and the Lansing and Y–SK strains. These strains were both isolated several years ago, the former from the brain of a fatal case in Lansing, Michigan,[10] in 1938, and the latter from the stool of an abortive case in New Haven, Connecticut,[11] in 1937.

Carrier Rate among Campers

An attempt was made to determine the carrier rate among the healthy members of the Blue Moccasin group. It may be assumed that the latter campers had the same opportunity for exposure as those who developed poliomyelitis. There had, of course, been contact between them. These data are presented in Table 2.

TABLE 2. *Presence of Virus in Stools and Throat Swabs.*

SOURCE	JULY 27–AUGUST 2 COLLECTION		AUGUST 5–14 COLLECTION		AUGUST 16–23 COLLECTION	
	STOOL	THROAT	STOOL	THROAT	STOOL	THROAT
Patients:						
Fi.	+	+				
Mo. }						
La. }	+					
He. }						
Mi.						
Healthy Blue Moccasin group:						
Be.	–	–			–	–
Dr.	–	–	+	–	+	–
Du.	–	–		–	+	–
Ha.		–	+	–	–	–
Ll.	–	–			–	–
Ry.	–	–				
Sv.	–	–				
Ti.	–	–			–	–
Ah.	–	–			–	–
Cr.	–	–			–	–
Cu.	+	+		–	+	–
De.	–	–			–	–
Ev.	–	–			–	–
Pe.	–	–			–	–
Po.			–	–	–	–
Pow.	–	–		–	–	
Wa.	+	–		–	–	
Pa.	–	–				
Home contacts of healthy carriers:						
M. Dr.			–	–	–	–
J. Cu.	–	–	–		–	
Remote contact campers:						
Fa.	–					
Ot.	–					
Be.	–					
Cus.	–					
Ja. }	–					
Jc. }	–					
Jk. }	–					

One of this group from whom specimens were collected developed the first symptoms of poliomyelitis one day after the first collection of samples. Both the stool sample and the throat swab collected at this time from this boy (Fi.) contained poliomyelitis virus.

Of the remaining members of the group, 5 virus carriers were found among 18 boys tested. All 5 were intestinal carriers, and only 1 of the 5 was found to harbor virus in the throat. None of them gave a history of symptoms compatible with the picture of mild poliomyelitis.

Of these 5 carriers, 3 were found to be excreting virus in the stools for a period of at least three or four weeks. Whereas the patient (Cu.) who was both a throat and intestinal carrier excreted virus in the stool for about a month, virus could no longer be found in the throat after the first week. These findings are analogous to those encountered in similar studies on the frequency and duration of virus carriers among patients with clinical poliomyelitis[1, 5] and in a similar camp group of healthy contacts.[2]

TABLE 3. *Humoral Neutralizing Antibodies to Lansing and Y–SK Strains in 3 Healthy Carriers of Virus and in 3 Healthy Controls Found Not to Be Carriers of Virus.*

SOURCE	SERUM ANTIBODY*		
Carriers of virus:	7/30/46	8/22/46	9/11/46
A	–	–	–
B	++	++	+++
C	+		++
Noncarriers of virus:			
D	++	++	++
E	–	–	–
F	–	–	–

*– = No demonstrable antibodies.
\+ = Undiluted serum neutralized virus.
++ = 10 x diluted serum neutralized virus.
+++ = 100 x diluted serum neutralized virus.
The amounts of virus used in these tests varied from 10 to 100 LD_{50} doses.

A small control group of 7 Pfd campers, not belonging to the Blue Moccasin group, were also tested. No intestinal carriers were found among them.

Carrier Rate among Secondary Contacts

Since the camp was officially closed and the boys sent home soon after cases occurred at the camp, an opportunity existed for studying secondary familial contacts, especially those of virus carriers.

Of the 5 healthy carriers, only 2 had siblings at home. Throat swabs and stools from both these siblings were collected over a period of a month. None of this material contained virus. It is of interest that one of these secondary contacts was exposed to a carrier harboring virus in the throat as well as in the intestinal tract.

Antibody Response to Murine-Adapted Strains of Virus

Although the Pfd strain did not appear to be related to the Lansing or Y–SK murine-adapted strains, neutralization tests in mice were carried out with the latter strains on serums from campers representing 3 healthy carriers of virus and 3 healthy controls who had been found not to be carriers of virus. Although neutralization tests with these murine-adapted strains had been carried out on hospitalized patients in other epidemics, antibodies had not here-

tofore been looked for in paired serums of healthy carriers collected early and late in relation to the time of virus excretion.

No significant change in antibodies to the murine-adapted strains as a result of exposure to the outbreak was demonstrable (Table 3). One of the carriers had no humoral antibodies and failed to develop any during the period of exposure. The serums of the other 2 carriers both contained antibodies at the time virus was first detected in the stools. There appeared to be a slight rise of questionable significance six weeks later.

Of the 3 healthy noncarriers of virus, 2 did not have humoral antibodies, nor did any develop during the interval of three to six weeks between collections. The third member of this group, on the other hand, maintained a constant antibody level during the six-week period.

Discussion

The attack rate in one group (the Blue Moccasin group) of Pfd campers was high. Of a total of about 31 campers, who were all, so far as is known, similarly exposed, 5 developed frank poliomyelitis, and of 18 healthy members of this group, 5 were found to be carriers. (The remaining 8 members were not available for study.) This gives a frank attack rate of about 5:31 (or 16 per cent) and an infection rate of 10:23 (or 43 per cent.) This high incidence of disease was recognized only among the Blue Moccasin group; no cases occurred in the two other groups living under almost the same conditions.

Of the 5 carriers, 3 excreted the virus in the stools for at least three or four weeks. These findings are analogous to those encountered in similar studies on the frequency and duration of virus carriers among patients with clinical poliomyelitis. Further study is necessary to determine the possible epidemiologic significance of the prolonged period of excretion of the virus from the intestinal tract. Of the 5 carriers who returned to their homes, only 2 had siblings there. Throat swabs and stool samples were obtained from both these children, and all samples gave negative tests in monkeys. It was unfortunate that this part of the study was so limited as to render our few negative results of no statistical significance.

Similarly, the serologic studies were disappointing, for the homologous strain was not used. In other words, the Pfd strain was not found to be related to the Lansing and Y–SK strains. Had the serologic studies been performed with the Pfd camp strain, an entirely different result might have been obtained. This was not feasible because of the failure of this strain to be adapted to rodents.

Summary

An outbreak of infantile paralysis in a boy-scout camp attended by boys aged twelve to eighteen years is described. Although the camp was divided into three groups the occurrence of clinical cases was confined to only one of the groups, and the carrier-rate studies were similarly confined to this group.

Of the 31 members of this group, 5 developed frank poliomyelitis, with 4 bulbar cases, 1 of which terminated fatally.

Of the 18 healthy members studied in this group, 5 were revealed to be intestinal carriers of virus, and 1 of these also harbored virus in the throat.

Estimates of the total infection rate in this group were roughly 43 per cent, with a ratio of frank cases to carriers of about 1:2.

Of the 5 carriers, 3 excreted the virus in the stools for at least three or four weeks.

In the single carrier in whom the virus was isolated from both the oropharynx and the intestinal tract, virus was isolated from the stools for a period of about one month; it could not be found in the throat after the first week.

In 1 of the clinical cases, virus was isolated from both the oropharynx and the stools one day before the onset of symptoms.

Of 2 siblings exposed to virus carriers (1 of whom had virus in both the throat and stools), neither subsequently became virus carriers.

The strain of poliomyelitis virus isolated during the outbreak did not appear to be related to the Lansing and Y–SK strains by serologic test, nor could it be adapted to rodents even after many trials.

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MEDICAL PROGRESS

THE "NEPHROTIC SYNDROME"*

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THE "nephrotic syndrome" is one of the most striking phenomena of renal disease. The combination of gross edema, hypoproteinemia, hypercholesterolemia, lipidemia and heavy proteinuria, in the absence of congestive heart failure, is unique and easily recognized. It frequently appears during the course of chronic diffuse glomerulonephritis (the nephrotic phase).[1] Other causes are renal amyloidosis, syphilis, intercapillary glomerulosclerosis and renal-vein thrombosis. In children and young adults the syndrome occasionally develops in the absence of renal disease as so-called "pure," "genuine" or lipoid nephrosis. A prolonged debate has centered about this entity. It is claimed on the one hand that the disorder is renal in origin, either a disease entity *sui generis*[2, 3] or the result of an unrecognized glomerulonephritis,[4, 5] and, on the other, that it is primarily extrarenal, perhaps on the basis of some obscure derangement of protein metabolism.[6, 7] Conflicting opinions regarding the pathogenesis of various manifestations are likewise unsettled, but there is general agreement that the "nephrotic syndrome" presents certain uniform and consistent features, whatever its etiology. The following discussion is devoted chiefly to a consideration of these aspects of the disorder.

PROTEINURIA

One of the most impressive and characteristic manifestations of the nephrotic syndrome is the continuous loss of large amounts of protein in the urine. The resulting drain upon body protein and the stimulus to increased protein synthesis probably contribute in the pathogenesis of various associated phenomena, but unfortunately, too few unequivocal facts are available at present to permit an analysis of the situation as a whole. Indeed, the nature and source of urinary protein is still debated, and current concepts of the renal mechanism of protein excretion are speculative.

Analysis of proteins in blood and urine is handicapped by the lack of satisfactory methods for isolating pure components of the protein mixture. Fractional "salting-out" precipitation has been used for separating albumin from globulin. It is now known that these fractions are heterogeneous. The use of ultracentrifugation, electrophoresis and immunologic technics indicates that at least five globulins and two albumins are distinguishable,[8–13] and it is believed by those intimately engaged in the work that even the refined fractions are not pure.[14] As Gutman[15] points out in an excellent review, the discovery that albumin obtained by fractional precipitation contains significant amounts of globulin is very important, since changes in the globulin content of the albumin fraction may account for apparent deviations from the normal.

The plasma protein composition is greatly altered in the nephrotic syndrome. All methods agree in revealing a marked reduction in albumin.[16, 17] The globulin content may rise, especially in amyloidosis,[18] remain unchanged or fall.[17, 18] Usually, the beta globulin and fibrinogen increase; the alpha globulin may rise when the albumin concentration is very low. Gamma globulin is almost always reduced.[18]

There is no reliable evidence that the plasma contains abnormal proteins. Plasma albumin, separated by precipitation, has a somewhat higher molecular weight and lower osmotic pressure than normal,[19, 20] presumably because there is a larger proportion of contaminating globulin. Differences in fractions obtained by ultracentrifugation may also be explained on this basis.[21] Specific antiserums to plasma albumin and globulin fail to precipitate nephrotic proteins quantitatively suggesting the presence of immunologically distinct proteins.[8, 22, 23] But it now appears that the unprecipitated portion of the albumin fraction is in reality globulin precipitated with the albumin during salting out. An abnormal distribution of globulins differing antigenically may be the cause of the anomalous behavior of nephrotic globulin.[8] Alving and Mirsky[24] found that nephrotic plasma from which globulin had been removed by precipitation contains less cystine than normal. They attributed this to the appearance of a cystine-poor albumin, from which normal albumin could be removed by recrystallization. It has recently been shown,[25] however, that alpha globulin, the usual contaminant, contains very little cystine, and it now seems likely that the authors were dealing with this component and not with an abnormal protein.

Albumin preponderates in the urinary protein mixture. The electrophoretic pattern may resemble the pattern of normal plasma in showing a very large albumin peak even when plasma albumin is markedly depressed.[19, 26] In some cases globulins may

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be prominent, apparently as a result of more extensive and severe renal damage.[27]

Evidence that abnormal proteins may appear in the urine has been vitiated by the failure to work with pure homogeneous fractions. It is interesting that the "abnormal" albumin detected in the urine by specific antiserums, by high molecular weight and by low cystine content is always present in lower concentration than in the plasma.[19, 24] Proteins of small molecular size predominate in the urine,[19] and it is consistent with this tendency that the "abnormal" protein, probably globulin, should not readily enter the urine. The evidence indicates that proteins are excreted on the basis of molecular size, configuration and electrical charge, rather than on the basis of some intrinsic abnormality of composition, suggesting mechanical filtration from the plasma as the mode of excretion.

Certainly, there is much in favor of the belief that urinary proteins are derived from plasma. It has long been known that proteins in plasma and urine are coagulated and precipitated in the same manner.[28] More recently it has been found that precipitated protein fractions from the plasma and urine of a patient with nephrosis are identical so far as the optical rotation, specific refraction, racemization, osmotic pressure, nitrogen distribution and immunologic properties are concerned.[22, 23, 29–32] Even though these studies have not been made upon pure fractions they establish beyond reasonable doubt the source of urinary protein. Hence it may be concluded that urinary proteins are derived from plasma by a filtration mechanism.

The obvious site of protein filtration is the glomerulus, where continuous ultrafiltration of plasma water and solutes has been shown to occur normally.[33, 34] The presence of precipitated protein in the glomeruli of patients with proteinuria lends further credibility to this view. There is nothing to suggest that tubular protein excretion plays a role, but it is possible that altered reabsorption may be important.

Normally, protein does not appear in the urine in concentrations greater than 9.0 mg. per 100 cc. or in amounts exceeding 150 mg. per day.[35] Thus, there is either insignificant passage of protein through the walls of the glomerular capillaries or almost complete removal of protein from the filtrate by tubular cellular activity. Samples of glomerular filtrate have been obtained in mammals by micropipette[34] and little or no protein detected, but the best methods available for the determination of proteins in such small volumes fail to show concentrations below 25 mg. per 100 cc.[36] Hence, it is possible that the human glomerulus produces a filtrate containing 20.0 mg. per 100 cc. and that, assuming a normal daily filtration volume of 175 liters, 35 gm. of protein may be made available in this way for possible loss in the urine. If these considerations are correct, a considerable proteinuria might develop as a result of a failure of tubular protein reabsorption. Even then, however, insufficient protein would be excreted to account for the huge losses — as much as 60 gm. per day[37, 38] — occasionally observed during the nephrotic syndrome. When it is remembered that, in addition, the plasma protein concentration is greatly reduced, with a lower filtrate concentration in consequence, and that the filtration rate may be less than normal, it becomes obvious that tubular dysfunction cannot be the sole basis for proteinuria. Increased filtration of protein must occur, apparently as a result of an alteration in the glomerular capillary walls rather than in the nature of plasma proteins. It is possible, of course, that reduced tubular reabsorption plays a contributory role, but the evidence presented below indicates enhanced rather than diminished protein reabsorption. Thus, regardless of etiology, proteinuria in the nephrotic syndrome is attributable to defective glomerular activity.

Alterations in Renal Structure and Function

The renal structural alterations associated with the nephrotic syndrome are exceedingly diverse and often obscure. There is a paucity of pathological material owing to the fact that most patients recover from the disease or progress into some more advanced phase before death. Cases have been reported singly or in very small groups.[39–43] In such studies no characteristic lesion has been marked out, and in a certain proportion of cases no renal disease has been found. As a rule, however, glomerular and tubular lesions are present.

The glomerulus is the logical center of attraction, but the search for lesions is often disappointing. According to Bell[5] and others,[44] the basement membrane is the most important component of the glomerular capillary wall since the endothelium is delicate, sparse and possibly not intact. There is a small amount of connective tissue between capillary loops forming a mesentery-like supporting structure often referred to as the "mesangium."[44, 45] A thin epithelial membrane covers the entire filtering surface, reaching in between capillary loops and dipping down into the spaces between the lobules. Thickening of the basement membrane, proliferation of the intercapillary connective tissue and piling up of endothelial cells (though the last is denied by MacCallum[46]) occur characteristically in chronic diffuse glomerulonephritis. During the nephrotic phase these changes are not extensive. In only a few glomeruli has the process resulted in hyalinization and obliteration.[5] Thus, the total area of the filtration bed is not greatly altered, although it is evident that the changes in the nature of the filter might be expected to result in a somewhat different filtrate composition. Similarly, in other disorders giving rise to the nephrotic syndrome glomerular lesions that do not appear to encroach seriously upon the filtering area are found. In amyloid disease,

there is a deposition of complex protein, possibly related in some manner to antibody production,[47] in the pericapillary spaces between the basement membrane and endothelium.[48] With progression, of course, compression of capillaries and obstruction to blood flow may lead to glomerular destruction. The renal disorder associated primarily with prolonged diabetes mellitus, intercapillary glomerulosclerosis,[5, 49–53] is characterized by the appearance of nodular masses believed to arise from sclerosis and hyalinization of intercapillary connective tissue. The capillaries are pushed apart, and the glomeruli may be strikingly deformed by this material. In contrast, the glomeruli in kidneys of patients, usually young children, dying during the course of lipoid nephrosis present few or no alterations. There may be some increase in the nuclear content of a few glomeruli, and adhesions between the tuft and Bowman's capsule may be demonstrable in some areas.[2, 5, 39–43] Bell[5] has reported diffuse thickening of the basement membranes in a few cases and claims to have found "pores" through which protein might escape into the urine. It is certain that there are no obvious glomerular lesions in many cases of the disorder. This is also true of the few cases of the nephrotic syndrome that have developed after thrombosis of the renal vein.[54, 55] The absence of glomerular lesions does not preclude capillary injury and increased protein filtration, however, since Walker and Oliver[34] found that protein appeared profusely in the filtrate after minor trauma to capillaries without visible injury.

The tubular pathology is almost always outstanding, after the disorder is well established.[56] Fatty and colloid substances appear as droplets or vacuoles in the tubule cells, particularly in the proximal segment. Nearly all the cells in this part of the nephron may be filled to bursting with brightly refractile fat.[57] The deposit is distributed irregularly, and groups of grossly swollen cells bulging out through the basement membrane may give rise to contortion and kinking of the tubules. In many places the nuclei are pyknotic, and there may be necrosis with desquamation of portions of the tubular epithelium. As a result of these changes, which occur in every type of the nephrotic syndrome, the kidneys become large, pale and rather yellowish and firm but not fibrotic. A few microscopic scars may be found scattered through the parenchyma, to a greater extent perhaps in the nephritic and amyloid forms, but rarely sufficient to cause grossly detectable fibrosis or contraction.

The source of the cellular inclusions typical of the nephrotic kidney is not settled. They were at first considered a result of cellular degeneration.[2] The demonstration that the lipid content of the kidneys is increased[58] appears to indicate, however, that intracellular fat is not unmasked by a change in physical state (fat phanerosis) but is deposited from without. The nature of the hyaline colloidal material has been elucidated by Gérard and Cordier,[59] Smetana and Johnson[60] and others who have approached the problem through comparative physiology. In the salamander a certain number of nephrons communicate directly with the peritoneal cavity, whereas others do not ("open" as opposed to "closed" nephrons). After intraperitoneal injection of solutions of various proteins bound to dyes and of nephrotic serums, brightly stained droplets of protein and doubly refractile bodies are found only in cells throughout the length of the open nephrons; none appear in cells of the closed nephrons. These findings support the conclusion that the reabsorption of protein and lipids from the glomerular filtrate by the tubules might account for the tubular pathology of the nephrotic syndrome. A similar phenomenon has been observed in mammals.[57, 61] Administration of protein-dye compounds to rats with proteinuria results in the appearance of deeply stained globules in the cells of the proximal segment. In the absence of proteinuria these substances do not pass into the urine, and tubular lesions do not develop.

Such data must be used cautiously in the interpretation of the tubular changes in nephrosis in man. There are excellent reasons for the belief that there is protein filtration, and it certainly seems probable that reabsorption of protein from the filtrate may induce certain alterations in cell structure. It is unknown, however, whether these changes are based upon overactivity of normally active reabsorptive mechanisms. Oliver[57] objects to the notion that the large, obviously destructive deposits of fat result from such overactivity because the deposits are irregularly dispersed. There is no information available regarding the distribution of reabsorbed protein in the tubular cells or its relation to fat infiltration. Fat tends to accumulate in injured cells,[62] and it is possible that a similar process occurs in the kidney after injury by excessive protein reabsorption. In the nephrotic syndrome the blood contains a high concentration of lipids in the colloidal state apparently forming large complexes with various globulins.[63] It is probable that such compounds are not readily filtered even when albumin traverses the glomerular membrane with ease. In line with this view is the low concentration of lipids in the urine, despite marked lipidemia.[64–66] That which appears in the urine seems chiefly to be contained within the desquamated tubular cells comprising the numerous urinary casts. Centrifugation of the urine removes most of the detectable lipids, apparently by removing this cellular debris. Hence it is not unlikely that fats and cholesterol enter the tubule cells from the blood rather than from the glomerular filtrate. Further study is necessary to answer this question.

The urine is often highly concentrated, containing cellular elements or casts of various kinds in great numbers. Erythrocytes, leukocytes and epithelial

cells may appear abundantly in the urine. Hematuria has been considered exceptional, but repeated examinations of the urine disclose showers of red cells from time to time in nearly every patient. Even in lipoid nephrosis, in which the absence of blood from the urine is regarded as a *sine qua non*, red cells are occasionally found. Casts are composed of coagulated protein, alone, or binding a heterogeneous mixture of cells and cellular material. In view of the high concentration of protein in nephrotic urine it is rather surprising that cast formation is not more impressive than it is. High concentrations of salts and urea have a dispersive influence upon proteins in solution, whereas reduction of the reaction of the glomerular filtrate during its passage down the tubule tends to favor precipitation.[57] There is some evidence that the introduction of a protein precipitant by tubule cells is necessary to disrupt these balancing influences, and to bring about protein coagulation.[57] Whether cast formation is restrained in the nephrotic syndrome by adequate concentrations of various dispersive solutes or by insufficient precipitant is unknown.

On the whole, kidney function appears to be excellent. Many writers have stressed the normality of concentrating power, phenolsulfonephthalein excretion and urea clearance and the absence of nitrogen retention, acidosis and other evidences of renal insufficiency.[2, 55, 56] Considering the state of the kidney it is not surprising that this should be so. Although glomerular lesions are demonstrable, there is little or no destruction of glomeruli. Hence filtration should not be greatly affected. The renal vascular system is relatively undisturbed, and blood continues to perfuse renal tissue normally. Although the tubular lesions may be striking, little loss of nephrons is incurred. Renal functional alterations are demonstrable only by more refined technics in most cases, particularly in lipoid nephrosis. Occasionally, however, the disturbance is more profound. Indeed, evidence of renal insufficiency develops sooner or later in most cases of the nephrotic syndrome in which progressive renal damage occurs, as in the course of chronic diffuse glomerulonephritis, intercapillary glomerulosclerosis and amyloidosis.

The glomerular filtration rate is usually reduced moderately, to values as low as 50 per cent of normal in many patients with chronic renal disease.[67–69] In children with lipoid nephrosis, on the other hand, the filtration rate may be increased markedly.[70–72] The urea clearance tends to follow filtration rate and to present similar decrements and increments. Although the possible causes of diminished filtration are obvious, it is difficult to explain the augmentation in children. Such a change may be the result of increased effective filtration pressure secondary to a vasomotor adjustment or to the fall in plasma oncotic pressure due to hypoproteinemia.

In the few cases studied thus far renal blood flow has been found within normal limits or slightly decreased.[67–69] In lipoid nephrosis elevations in blood flow have been reported.[72, 73] What these changes may imply regarding vasomotor activity within the kidney we cannot at present state with any certainty.

Tubular function is usually unaffected. Various measurements, such as those by glucose, Diodrast and para-aminohippurate Tm, tend to be normal despite the reduction in filtration.[69] Thus, the stream of urine may flow more slowly down the tubule, prolonging its contact with active reabsorptive cells and providing an improved opportunity for reabsorption of water and solutes. This phenomenon of glomerulotubular imbalance may account for continued normality of concentrating power and for occasional fixation of urinary specific gravity at a high level. It is possible, too, that urea reabsorption may be enhanced in this manner to give rise to the modest elevation in blood urea sometimes observed. Certainly, the tubule cells appear to acquit themselves well. Not only can they reabsorb water and electrolytes normally or even in excess but also they are capable of adequate excretion of hydrogen ion and of ammonia synthesis.

Renal functional and anatomic abnormalities are thus demonstrable in every case of the nephrotic syndrome. They vary considerably in kind and degree, but are never so severe as to suggest extensive damage and loss of tissue. These processes are characteristically reversible. Every trace of the disorder may disappear, and the kidneys return to normal in many patients, even after a prolonged illness. In others, however, parenchymal damage may finally ensue with the development of renal insufficiency as nephrons disappear and the glomerular filtration bed shrinks. In this process the nephrotic syndrome clears.[55, 56] Proteinuria is less marked and may ultimately cease altogether, apparently as a result of the obliteration of defective glomeruli and the diminution in the available filtration surface through which protein may escape from the blood. As protein loss diminishes, the plasma protein concentration rises and peripheral edema regresses.

(To be concluded)

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

BENJAMIN CASTLEMAN, M.D., *Associate Editor*

EDITH E. PARRIS, *Assistant Editor*

CASE 34071

PRESENTATION OF CASE

A fifty-seven-year-old man entered the hospital because of a lump in the right upper quadrant.

The patient's attention was first called to his abdomen three weeks prior to admission when he had an acute pain in the region of the umbilicus while attempting to lift a plank. The pain persisted for two hours and then disappeared completely; it was not accompanied by nausea, vomiting or other gastrointestinal symptoms. At that time he noted the mass, which was tender and which in the following three weeks grew slightly larger and moved up and to the right. Following the discovery of the mass he limited his food intake, and his bowel movements became somewhat more scanty, having previously been regular. The only change noted in the character of the stools was that they were perhaps somewhat lighter in color. An estimated 10 to 15 pounds of weight had been lost during the present illness.

The patient had been addicted to morphine for thirty-seven years, a habit initiated by taking the drug for several attacks of right-lower-quadrant pain diagnosed at the time as chronic appendicitis. Six major and numerous minor attempts were unsuccessful in breaking the habit.

Physical examination showed a slender, rather nervous man. There were numerous injection scars on the arms and thighs. Examination of the heart and lungs revealed only emphysema. The abdomen was flat and soft throughout. In the right upper quadrant there was an irregular, firm, movable, tender mass, 8 by 6 cm. in diameter, which appeared to be attached posteriorly but was thought not to be connected to the liver.

The temperature, pulse and respirations were normal. The blood pressure was 160 systolic, 85 diastolic.

Examination of the blood showed a hemoglobin of 13.5 gm. and a white-cell count of 10,400. The urine was normal. Two stool specimens were guaiac negative. The nonprotein nitrogen was 31 mg. per 100 cc., the total protein 8.18 gm., with 4.53 gm. of albumin and 3.65 gm. of globulin, the phosphorus 3.5 mg. and the phosphatase 4.9 units. The van den Bergh reaction was normal, and the cephalin flocculation test +++ in twenty-four and forty-eight hours.

An x-ray film of the chest disclosed findings consistent with emphysema; a barium enema showed no evidence of disease intrinsic to the large bowel and no evidence of external compression; an intravenous pyelogram demonstrated no evidence of disease of the urinary tract, a gastrointestinal series was not completely satisfactory but no abnormalities were made out, and a cholecystogram showed no definite evidence of a gall-bladder shadow. On one film the right kidney and its pedicle were seen to be outlined more clearly than usual.

On the tenth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. RICHARD H. SWEET: As we progress with this history the real decision that we have to make is whether the tumor, which was very obvious in the patient's abdomen, had anything to do with the trauma that is described, because the record mentions that the patient's attention was first called to the abdomen when he had acute pain in the region of the umbilicus while attempting to lift a plank. It is a very short history. I do not know whether he was a good plank lifter or not, but people accustomed to lifting heavy weight know how to do it, so that they do not rupture a deep epigastric artery and cause abdominal-wall tumors of traumatic origin. I am rather inclined to discount the trauma. At any rate he felt the pain and this pain was short-lived — lasting only two hours in duration and disappearing completely — and we assume that it never came back.

"Following the discovery of the mass he limited his food intake." That statement makes no sense, since it does not reveal why he limited the food intake. He had no nausea or vomiting, and was supposed to feel well. Limitation of food intake is unusual simply because a patient feels something in the abdomen. Perhaps his doctor had something to do with it.

The fact that the patient was a morphine addict is important, because I believe that it makes the history completely unreliable. I have never seen a morphine addict who could tell a straight story about anything, especially about his own symptoms. That discourages me. I do not consider this history worth anything in the making of a correct diagnosis.

I should say that the laboratory findings were within the normal range. I imagine that liver disease was looked for, and I assume that there was no evidence of it.

I also assume that the gastrointestinal series was not repeated even though it was not satisfactory. I suppose that the cholecystogram revealed a shadow, but the examiners were not sure of it; it was not definite. That is the only thing about the x-ray examination that interests me.

On one film the right kidney and its pedicle were seen to be outlined more clearly than usual. I do not understand what that means. Did the patient have some retroperitoneal gas or some air outlining the kidney and its pedicle? That is unusual to see, is it not, Dr. Wyman?

DR. STANLEY M. WYMAN: Yes. The chest is clear but shows emphysema. The patient did have two gastrointestinal examinations. They show a normal-appearing stomach and duodenal bulb and loop. There is a little calcification in the left upper quadrant, which probably lies in the splenic vessels. On one of these films that cannot be seen clearly, there is a somewhat irregular pattern of the esophagus, which makes me raise the question of possible varices. I cannot make a definite statement because the film is not sufficiently good.

DR. SWEET: You do not see any definite mass?

DR. WYMAN: The right colon is pushed down somewhat. That may be a large liver, or possibly a mass that cannot be outlined.

DR. SWEET: I think it is stated somewhere that the mass was attached posteriorly and that it was not connected to the liver. That is an important observation, if we are going to decide what this mass might be. The statement may be correct; it may not be. I know that I can make that error myself. I have occasionally seen an enormous hydrops of the gall bladder in which the fundus of the gall bladder felt very much like an ovarian cyst lying in the right lower quadrant of the abdomen. The problem resolves itself into a very simple matter of deciding what the abdominal tumor was. Presumably it was of short duration and was easily felt by the physicians in attendance. It was a hard, irregular, movable mass not connected with the liver but attached posteriorly. The gall bladder is usually smooth and not irregular, unless it is involved in carcinoma. It is almost always attached to the liver. A carcinoma of the duodenum is excluded by the x-ray findings, as is carcinoma of the pancreas. A renal-cell carcinoma would also have shown some abnormality of the kidney shadow in the intravenous pyelogram. Carcinoma or other tumor of the hepatic flexure ought to be thought of, but there again the x-ray film ought to exclude it. That brings us down to the assumption that this tumor was retroperitoneal, one of those unusual mesenteric cysts, or something of that sort. But it was hard and irregular, so that we might on that basis exclude such a diagnosis. I should like to mention lymphoma, but the retroperitoneal lymphomas that we see are usually farther over to the midline, almost always fairly fixed in the posterior aspect of the abdomen.

I should like to return again to the question of trauma, because I should at least mention the possibility that there was a hematoma from a ruptured vessel from lifting the plank. Trauma of that sort is most apt to cause rupture of the deep epigastric artery, and then of course the tumor lies in the rectus sheath. In that case the patient has excruciating pain, which does not disappear in two hours. It brings the patient into the hospital. An emergency operation is often performed because the pain is so intense, although the diagnosis may not be made ahead of time.

Having mentioned most of the possibilities that I can think of I am inclined to agree that this was a surgical case and that the patient should have been operated on, but I think it is very presumptuous to attempt to make a diagnosis.

DR. BENJAMIN CASTLEMAN: Does anyone want to offer to make a more definite diagnosis?

DR. WYMAN: I wonder if Dr. Sweet would consider the possibility of hepatoma very strongly.

DR. SWEET: Yes; I intended to speak of that. Tumor of the liver, although the mass is not connected with the liver on physical examination, should be mentioned — a tumor hanging from the liver on a pedicle. I have actually removed such a tumor.

DR. WYMAN: My reason for mentioning hepatoma is that if the esophageal irregularity proved to be varices, that diagnosis might offer a lead.

DR. SWEET: I excluded that possibility because the gastrointestinal tract was normal.

CLINICAL DIAGNOSIS

Carcinoma of gall bladder?
Carcinoma of bile ducts?

DR. SWEET'S DIAGNOSIS

Morphinism.

ANATOMICAL DIAGNOSES

Subacute and chronic cholecystitis, with perforation.
Cholelithiasis.

PATHOLOGICAL DISCUSSION

DR. THOMAS GEPHART: We were confused, of course, by the history. We did have the advantage of peritoneoscopy before operation, which is not included in the record. That was reported by Dr. Benedict as showing a mass in the right upper quadrant. We could not be sure whether it was retroperitoneal or an enlarged, inflamed gall bladder. I might say that on examining the patient in the

ward this mass was well below the liver edge and did not seem to move with the liver, although he did not have, as I remember it, marked excursion of the liver on inspiration and expiration.

At operation we explored the right upper quadrant, and on opening the abdomen we found a large mass covered with omentum extending down the right side of the abdomen. It was found to be attached to the transverse colon, and when it was freed, it became obvious that it was an acutely and chronically inflamed gall bladder, the thickened wall extending to the level of the umbilicus. When we first felt it, it was so hard that we thought that it was carcinoma. On freeing it from the omentum, we broke into it, and a large amount of yellow pus escaped. It was necessary to free it from the transverse colon with sharp dissection, and we found numerous stones, one of which — a large one — was impacted in the ampulla of the gall bladder at the beginning of the cystic duct. In retrospect, putting the picture together, we thought that the patient had an inflamed gall bladder completely masked by the morphine addiction; probably, as he lifted the plank the gall bladder ruptured and he developed a localized peritonitis, which fortunately for him he was able to tolerate well. The wall of the gall bladder in one place was 2 cm. thick. After we removed it we asked the laboratory to do a frozen section, and there was no evidence of carcinoma.

DR. CASTLEMAN: There was a piece of tissue removed from outside the gall bladder that showed a gallstone surrounded by foreign-body reaction, so that we have proof that the gall bladder had perforated, probably after the patient lifted the plank three weeks previously. The wall showed a subacute and chronic inflammatory reaction but no carcinoma.

CASE 34072

PRESENTATION OF CASE

A forty-one-year-old gasoline-station operator entered the hospital complaining of boring epigastric pain.

Five years prior to admission the patient first experienced pain in the epigastrium, occurring after meals and relieved by food or alkali. A Graham test two years before admission failed to visualize the gall bladder. Following this, an operation was done, and the gall bladder was not found. An appendectomy was performed. The pain reappeared after a year's alleviation following operation. He had been eating "anything and everything."

Physical examination of the chest and abdomen was negative; there was a healed scar over the right rectus muscle.

The blood pressure was 130 systolic, 85 diastolic.

Examination of the blood disclosed a hemoglobin of 15.3 gm. and a white-cell count of 10,900. Urinalysis gave a specific gravity of 1.012, and was negative for sugar, albumin and diacetic acid; rare white cells and epithelial cells were seen in the urinary sediment. A gastrointestinal series showed enlargement of the gastric rugal folds. The duodenal bulb was constantly deformed and showed pooling of barium in the midportion, with a surrounding area of rarefaction, consistent with edema about a crater.

On the fifth hospital day a subtotal gastrectomy, with a gastrojejunostomy, was done. Two days later the patient's condition was "alarming," with low blood pressure, a thin rapid pulse, peripheral vascular collapse and cyanosis. The temperature was 102°F. orally. The chest was clear. The abdomen was silent and only slightly distended. Penicillin and streptomycin were started. Following this, he passed very little urine, and the nonprotein nitrogen rose to 110 mg. per 100 cc. on the third postoperative day. Because of tenderness and spasticity in the right upper quadrant an incision was made and about 1000 cc. of "grossly uninfected bile" was drained. On the fifth day, following the original operation, the temperature remained elevated, and the nonprotein nitrogen rose to 165 mg. per 100 cc. The serum amylase was reported as 100 units, and atelectatic areas were visualized at the right base by x-ray examination. The patient expired on the eighth day following the original operation.

The fluid exchange during and after the operation was as follows:

	INTAKE		OUTPUT	
	INTRAVENOUS	ORAL	URINE	LEVINE TUBE
	cc.	*cc.*	*cc.*	*cc.*
Day of operation:				
Transfusion	1000			
5 per cent dextrose in water	1500			
5 per cent dextrose in physiologic saline solution	1000	0	Unknown	0
First day:				
5 per cent dextrose in water	1200			
10 per cent Amigen	1000	360	120	1000
Second day:				
Transfusion	500			
10 per cent Amigen	1000			30
Third day:				
Transfusion	500			
5 per cent dextrose in physiologic saline solution	300			
5 per cent dextrose in water	1300		120	750
Fourth day:				
Transfusion	500			
5 per cent dextrose in physiologic saline solution	500			
5 per cent dextrose in water	2200			720+
10 per cent Amigen	1000			2000*
Physiologic saline solution	100		470	
Fifth day:				
5 per cent dextrose in physiologic saline solution	1600			
5 per cent dextrose in water	1500		850	750
Amigen	900			

*Estimated amount lost at time of incision and drainage.

	Intake		Output	
	Intravenous	Oral	Urine	Levine tube
	cc.	cc.	cc.	cc.
Sixth day:				
5 per cent dextrose in physiologic saline solution	1700			
5 per cent dextrose in water	500			
5 per cent Amigen	1000		1250	240
Seventh day:				
5 per cent dextrose in physiologic saline solution	2300			
5 per cent dextrose in water	500		1630	Unknown
Eighth day:				
5 per cent dextrose in physiologic saline solution	500			
5 per cent dextrose in water	2700	1250	1580	690

Differential Diagnosis

Dr. Charles L. Short: May we see the x-ray films?

Dr. Stanley M. Wyman: There is a small hiatus hernia seen on all films. There is slight prominence of the gastric rugae. The duodenal cap is strikingly deformed, constantly throughout two examinations. The small pool of barium seen proximally in the cap may represent a crater or possibly barium caught between folds. The duodenal loop is normal in size and contour. There is no evidence of excretion of the gall-bladder dye on one examination. The postoperative film of the chest taken with a portable apparatus shows atelectasis at both bases, but clear lung fields otherwise.

Dr. Short: Would you say that a definite ulcer crater was demonstrated?

Dr. Wyman: In going back over the films, I am not entirely convinced that it is. I think that it might perhaps more readily be interpreted as barium between folds for the reason that the contour appears to change and a crater would remain constant.

Dr. Short: Do you see any air or barium in the biliary tree?

Dr. Wyman: No; I do not.

Dr. Short: Do you think that these defects could be caused by adhesions outside the duodenum, such as pericholecystitis?

Dr. Wyman: They are more consistent with a deformed cap from an old duodenal ulcer.

Dr. Short: We have a reasonably certain x-ray diagnosis, then, of an active duodenal ulcer, although the roentgenologist is not quite willing to say that the picture is absolutely diagnostic. The patient's history seems typical of this condition, including a year of remission of symptoms. Perhaps a different history given two years before directed attention toward the gall bladder, and at that time a positive Graham test was obtained.

The next statement is a surprising one — that the gall bladder was not found at operation. I can think of three possible explanations for this, although there may be more. The patient may have had congenital absence of the gall bladder. This is a rare condition, but cases have been recorded. The second is that the gall bladder occupied an anomalous position, perhaps embedded deep in the liver, or was covered by a congenital band. The most likely possibility, I think, is that identification of the gall bladder was difficult on account of adhesions in that neighborhood. In view of the x-ray findings the source of the adhesions may well have been a healed perforation of a duodenal ulcer, although we must still bear in mind the possibility that the patient had cholecystitis. Physical examination is not helpful, and the urinalysis gives no hint of underlying renal disease. We can assume that the preoperative diagnosis was duodenal ulcer and that the indications for operation were that the patient was unable or unlikely to follow a medical regime. Since a gastric resection was performed, fairly good evidence of duodenal ulcer must have been found at operation. I shall be interested in hearing later more details of the findings, especially regarding the presence or absence of the gall bladder and of adhesions in that area.

Two days after operation the patient's condition suddenly became worse, with the development of fever and a state of shock. Examination of the abdomen revealed the development of at least a localized peritonitis. In view of the drainage of large amounts of bile two days later, it seems to me that the conclusion is inevitable that the patient had peritonitis that had arisen at the duodenal stump, either from leakage or from actual rupture. A more remote possibility is that the patient actually had gallstones and that one had ruptured through the gall bladder or common duct with the development of bile peritonitis. Acute pancreatitis is another possibility. Certainly it would be a rare complication of an operation in this area. I do not see how one could make that diagnosis from the evidence at hand. I do not believe that the elevated serum amylase is significant in view of the degree of renal failure. If we accept any of the diagnoses I have mentioned, the absence of pain at the time of this catastrophe would be unusual. In view of the history and x-ray films and the findings at operation, I shall assume that the patient did not have cholecystitis and am willing to eliminate that diagnosis.

We can only speculate regarding the cause of the duodenal leakage. From the figures that we are given on fluid exchange I do not believe that we can say that the patient was given too much water and salt immediately after operation, with the consequent development of edema and obstruction in the region of the stoma. Following the development of peritonitis the patient's course was marked by anuria succeeded by oliguria and the gradual resumption of a respectable urinary output. Except for the fourth postoperative day, when drainage was done, he maintained a positive fluid balance. The nonprotein nitrogen rose rapidly, however,

reaching 165 mg. per 100 cc. by the fifth postoperative day. The amount of fluid lost through external drainage is not recorded after the first day, and he undoubtedly continued to lose large amounts of fluid, electrolytes and protein through exudation into the peritoneal cavity. It is possible that the azotemia was due to the extrarenal causes I have mentioned, but more likely to some form of severe renal damage. I am referring to lower-nephron nephrosis, the common etiologic factors of which are shock, intravascular hemolysis and sulfonamide toxicity. He certainly went through a period of shock; intravascular hemolysis is possible since he received 1000 cc. of blood, but we have no record of sulfonamide administration. Further data on the blood chemistry would be of interest but not diagnostic. The urinary findings, especially his ability to concentrate, would also be helpful. He evidently did not develop obvious edema, and we have no record of a blood-pressure rise before death.

It is hard to decide whether he died from sepsis or renal failure — probably a combination of the two. It is possible that he might have pulled through in the absence of peritonitis since he had an adequate urinary output in the last three days. It is difficult from the data at hand and without seeing the patient to comment on the fluid therapy that was employed. The amount of salt and fluid given the patient following the development of anuria seems contrary to the accepted principles of tiding over a patient with lower-nephron nephrosis with minimal amounts of both until renal function is resumed. But this patient in view of losses through drainage and exudation seemed to need more fluid and salt than the 500 to 1000 cc., including 300 cc. of physiologic saline solution, which is usually prescribed by those who have studied this type of renal damage. However, I think that therapy may have been a little too enthusiastic and that some edema of the lung and other tissues was found at autopsy. In conclusion, I shall offer the following diagnoses: duodenal ulcer, bile peritonitis secondary to leakage from the duodenal stump and lower-nephron nephrosis.

Dr. Tracy B. Mallory: Dr. Welch, will you discuss the operative findings?

Dr. Claude E. Welch: The treatment that the patient had before he came to the hospital represented a long series of medical attempts with alkalies and bland diet, with never any relief of symptoms, so that he was very unhappy about the situation and something was needed surgically. We believed that there was a certain amount of difficulty in making a clear-cut diagnosis, especially in view of the previous surgical findings. Therefore, I decided to do a laparotomy with a gastric resection, if he turned out to have an ulcer, rather than a transthoracic vagotomy. He turned out to have a large duodenal ulcer, one that was nonresectable. In other words, it involved the whole first and second portions of the duodenum, running down to the common duct. Consequently, I elected to do a procedure that was originally described by Finsterer[1] and later by Wilmanns[2] and others, in which the stomach is transected proximal to the pylorus, the entire mucous membrane of the pyloric segment removed and the muscularis of the stomach closed. One of the difficulties of this type of operation is the danger of leakage from the gastric stump, which does not heal so well as the duodenum. To date we have had no fatality from this course, and the operation has been carried out in 30 or 40 cases. The blood supply seemed to be extraordinarily good at the time, and we were successful in getting an excellent closure.

The postoperative course was of interest, and Dr. Short has analyzed it very accurately. A great deal of blood chemical study was done but not recorded in the printed summary. It became obvious at the end of sixty hours that the patient was not doing well. There was a lengthy discussion regarding whether to do an exploratory incision at that time to discover the cause of the trouble. An exploration was carried out, and bile peritonitis, presumably from a leak of the gastric stump, was found. Thereafter fluids were given in accordance with the blood chemical findings. The chloride was almost constantly low, which explains the fact that he received a rather high intake of chlorides.

Dr. Benjamin Castleman: What about the gall bladder?

Dr. Welch: I could not find it at the time of operation.

Dr. Short: If the diagnosis of lower-nephron nephrosis is correct, the low chloride might have been explained on the basis of increased plasma volume.

Dr. Welch: A tremendous amount of chloride was being lost through the abdominal drainage; it could not be accurately estimated.

DR. JACOB LERMAN: A certain amount of Amigen sometimes elevates the nitrogen faster than it can be excreted in the urine. It may be just a temporary situation.

DR. MALLORY: The patient had a definite oliguria that lasted four days, an output below 500 cc. on each of these days, and this figure is the minimum output that will clear nitrogenous waste products.

CLINICAL DIAGNOSES

Bile peritonitis.
(Duodenal ulcer).

DR. SHORT'S DIAGNOSES

Duodenal ulcer.
Bile peritonitis, secondary to leakage from duodenal stump.
Lower-nephron nephrosis.

ANATOMICAL DIAGNOSES

Duodenal ulcer, chronic.
Operative wound, gastric resection and gastroenterostomy.
Perforation of pyloric stump.
Peritonitis, generalized, acute, with fat necrosis.
Lower-nephron nephrosis, healing.
Congenital anomaly — absence of gall bladder.

PATHOLOGICAL DISCUSSION

DR. MALLORY: Autopsy showed, as was expected, a perforation of the stump of the gastrectomy. There was an old scarred duodenal ulcer. There was no gall bladder. There was a slight diffuse peritonitis accompanied by many foci of fat necrosis throughout the peritoneal cavity, indicating that duodenal contents had made their way around through the gastroenterostomy and the perforation in the pyloric stump.

The kidneys were significantly enlarged, the combined weight being 450 gm. Microscopically they were interesting to me because they showed a subsiding but definite lower-nephron nephrosis as Dr. Short predicted. In these cases the tubules are usually rather massively blocked with hemoglobinuric casts. In this case only traces were left. On the other hand there were well marked degenerative changes in the epithelial cells of the lower segments of the nephron. There was the usual interstitial inflammation between the straight tubules, most marked at the junction of the cortex and medulla, and there were some of the interstitial granulomas that are frequently seen from the fourth to the fifth day in lower-nephron nephrosis. There was also a definite degree of cloudy swelling in the proximal tubules, which I think is not a characteristic part of the picture although there is some difference of opinion about that. So far as the kidneys were concerned, I believe that the patient could have survived. He had gone through the acute stage and had re-established fairly adequate urinary output, and the histologic picture in the kidney corresponds with that very closely. This was evidently a healing lesion.

DR. SHORT: Were the lungs edematous?

DR. MALLORY: There was only slight pulmonary edema. There was nearly 2 liters of fluid in the abdomen.

A PHYSICIAN: Did the fluid contain much bile?

DR. MALLORY: At the time of autopsy it was not so darkly bile stained as the fluid previously drained.

DR. SHORT: From the autopsy findings parenteral fluid and salt were certainly not given in excess.

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Communications should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston 15, Massachusetts.

BLUE CROSS

Much has been said and a great deal has been written during the past year about Blue Cross plans and their difficulties. In view of certain doubts and confusions that have arisen, it seems not only opportune but also most fitting that a careful analysis be made of a service that now makes available hospital care for almost thirty million of the American population.

It is essential to have in mind the purpose of the founding fathers of Blue Cross. This may be summarized as an effort to provide financial protection against the hazards of unpredictable illness, and the plans have been exceedingly helpful to their subscribers in making this protection possible through the years of Blue Cross existence. Until caught in the spiral of inflation, the plans have been helpful to hospitals by guaranteeing reimbursement, with the advantage of an assured source of income, which has made budgetary planning, in a degree, easier and more secure. The importance of this factor can be better appreciated when one realizes that from 40 to 60 per cent of persons hospitalized in Massachusetts are Blue Cross subscribers. In view of this fact, Blue Cross must justifiably be considered a valuable voluntary instrument for protection against all, or part, of the hospital bill.

Varying methods of reimbursement to hospitals are in vogue throughout the country. Some are on the basis of established hospital charges, some on costs, and others in accordance with a previously agreed rate. Last June there was adopted in Massachusetts what is termed an all-inclusive plan — namely, the furnishing to the subscriber of almost his total hospital needs. In the face of the continuing increases in the cost of hospital operation, this change played its part in the development of the present unsatisfactory situation. This is explained by the fact that whereas the costs were increasing, both subscription rates to subscribers and reimbursements to hospitals were expected to remain fixed for a period of a year. Factors of influence in Massachusetts that add to Blue Cross financial difficulties are a high incidence of admissions and a longer average hospital stay than occurs under other Blue Cross plans, with a consequent serious drain on Blue Cross financial resources.

The public, the hospitals and the medical profession must all play their part in the preservation of Blue Cross. To do this calls for cold, keen and careful analysis. The fear of increasing Blue Cross subscription rates must not be exaggerated or overemphasized, for the American public is conscious of increasing costs in every line of endeavor and has shown its willingness to pay for what it receives. The zeal for maximum enrollment of subscribers on the part of those charged with this responsibility must not overshadow actuarial safety and sound financial management. Through it all, thinking and planning must be along a specific line — namely, the best interests of the public, which, after all, pays the bills. In exercising this concern and interest, the solvency of both the hospital and Blue Cross must be protected.

It is not too much to ask on behalf of the hospitals that Blue Cross subscribers do not add materially to their financial burdens. In the interests of mutual interdependence, it must be remembered that it is vital to the success of Blue Cross plans that hospitals remain financially sound, and it is not wise, when plans for the provision of voluntary care are extended, that either Blue Cross or hospitals should sustain financial losses. In the long run this must spell insolvency for one or the other, or both. If Blue Cross is to sell good hospital care, hospitals must be adequately compensated for furnishing that care. We cannot, therefore, escape the basic principle that the consumer, for whom the plan is provided, must pay an adequate premium or assume some portion of the risk that makes possible the service that he receives.

In conclusion, although it must be confessed that all is not well, it must also be realized that the patient (in this instance, Blue Cross) is not beyond cure and will be restored to health and usefulness if the public, the Blue Cross itself, the hospitals and the medical profession all do their part. If Blue Cross is to continue, as it should and *must*, the hospitals must support it staunchly, and those responsible for Blue Cross policy and management must be ever mindful that hospitals cannot endure without adequate reimbursement for the services that they render.

HELP FOR THE EPILEPTIC PATIENT

ELSEWHERE in this issue of the *Journal* a survey by the American Epilepsy League entitled "Who Cares for the Epileptic?" deals with the persons with seizures (more than 90 per cent) who are treated — if treated at all — by physicians in private office or in clinic. The survey does not deal with two other important aspects of epilepsy: the care of the minority group in tax-supported hospitals, and the interest of the general public in this segment of the sick population.

The year 1948 marks the semicentennial of the opening of the Monson State Hospital for epileptic patients, near Palmer, Massachusetts. Dr. William N. Bullard, backed by the Massachusetts Medical Society, provided the impetus for this project. The third colony in the United States specifically for the care of epileptic patients, Monson is probably second to none in the effective use of available resources. However, the facilities both in capacity and in personnel are sadly inadequate to meet the demand. Physicians, parents of patients or patients themselves look despairingly at the long line of applicants waiting for months or years before doors that seldom open. Neither the parents manacled to a defective, seizure-ridden and perhaps unmanageable child nor the adult patients who are sound of muscle and mind but cannot keep a job because of uncontrolled convulsions are in a position to complain of the sort of physical and medical care that costs a total of less than $1.50 a day, including less than 40 cents a day for food. (In sharp contrast, the amount paid by taxpayers for the hospitalization of epileptic veterans is approximately ten times greater.)

The obvious solution to the plight of the hundreds of waiting patients is more beds (in which there has been no increase at Monson for more than twenty years) with, of course, a larger budget both to maintain the beds and to provide wages high enough to attract personnel. However, the present yearly cost of institutionalized epileptic patients in Massachusetts is already in excess of a million dollars, and dispensers of public funds will want to know the causes for the present congestion and whether other alleviating measures might also be instituted.

The subject merits a broad and disinterested study, but two causes of congestion are immediately apparent. With bed space static, new patients cannot enter unless old ones leave. Thanks very largely to the development of the electroencephalograph and of more effective drugs in the last two decades, the control of seizures has been vastly improved. An increased turnover of institutionalized patients might be anticipated, but the present combined death and discharge rate of approximately 10 per cent is less than half the rate that obtained in the bromide period thirty years ago. Instead of developing a more rapidly moving stream of patients entering and leaving, epileptic colonies are becoming stagnant pools. Advanced medical care given to the hopelessly defective and a lack of social science

for the hopeful patients tend to block the exits of the institution. The lives of imbecile children with brains undeveloped or irreparably damaged, whose only hope is death, are prolonged through the conscientious use of prophylactic inoculations against childhood infections. Thanks to the sulfonamides and penicillin, pneumonia is no longer the friend of the aged to the extent that it once was. Tuberculosis, formerly a 10 or 12 per cent contributor to death in institutions, is under control at Monson. A recent survey by means of chest films disclosed less tuberculosis than in the outside population.

However, the decrease in exits because of death has been less in recent decades than the decline in the discharge of living (usually improved) patients. One reason may be the retention of the more able adult patients, which helps to keep down the cost of services. Doubtless a careful survey of patients would disclose a number whose seizures are under control and who might return to the family or the community and make way for patients more urgently in need of hospital care. Such a survey and resulting placements would require the professional help of social workers. At present the hospital staff and the 1400 patients have not a single social worker to help them in their multiplied social problems, although formerly Monson was adequately supplied — a circumstance that may account for the greater rate of discharge at one time. Doubtless each dollar spent in salary and adequate working conditions for competent social workers would save many dollars now lost through a stagnating pool of patients. A "total push" method of medical and social therapy would probably enlarge the outlets of the pool and permit the entrance of actively epileptic adult patients able to do the work of those discharged. During the past year, deaths numbered 54, and discharges 74. The total of 128 is approximately 10 per cent of the patients, which means residence for an average period of ten years, at a total cost per patient of at least $5000, of which approximately $250 is paid by the patient or his family.

However, the greatest long-range saving of money and release from the pressure of applicants should come from decreased need for institutionalization. As a money and health saver, prevention far outmeasures treatment, especially in epilepsy, in which a few capsules of medicine a day may mean the difference between social dependence and independence. Early diagnosis and institution of proper medical and social therapy for patients would prevent many a patient from ever entering Monson and becoming a public charge. Massachusetts has led the world in research, in drug therapy and in lay support of epileptic patients. In recognition of this fact, a National Veterans Epilepsy Center has been established at the Cushing Veterans Administration Hospital at Framingham. Establishment of a somewhat similar preventorium of chronic epilepsy and its sequelae near a center of medical influence for the short-term treatment, education or training of young persons of good intelligence would be a pioneer and profitable investment of public money. Contact with this group of patients, whose prognosis regarding both seizures and social usefulness is good, would increase the interest and the spirit of the medical, nursing and social-therapy staffs of Monson.

The second domain of importance for epilepsy and the most fundamental to the proper care of patients is the attitude of the general public. When the public realizes how much can be saved in dollars and in tears through medical research, through early and intelligent treatment of persons subject to seizures and through preventive measures intelligently applied (eugenics, better obstetrics, fewer childhood infections and fewer industrial, automobile and war injuries) enterprises now only dreams will quickly become facts. Experience has shown that public sentiment is changed only when groups of interested persons deadly in earnest get behind a program of enlightenment. This has happened for the epileptic patient in the organization of the American Epilepsy League, with an affiliated New England chapter with headquarters at 50 State Street, Boston. The New England Epilepsy League, which acts as a leaven in the otherwise unresponsive dough of public opinion, inspired the survey of Massachusetts doctors reported in this issue of the *Journal*, as well as a survey of all schools of higher education in the United States reported in the current issue of *Epilepsia*. It seeks to overcome prejudice among educators and employers and to aid phy-

sicians in their care of patients, whether private, clinic or institutional. It would lend its experience and knowledge to any broad-visioned, long-term plan for the prevention and better treatment of epilepsy, with consequent saving of both money and socially useful lives.

THE NOLEN-MILES POUND LAW

ATTENTION is called to the communication by Dr. John Conlin, director of medical information and education of the Massachusetts Medical Society, which appears on the following page. It is of paramount interest to all physicians. Senate Bill 264 is pending before the General Court of the Commonwealth of Massachusetts. This legislation, entitled "An act to make available unclaimed and unredeemed animals impounded in animal pounds for scientific investigation, experiment or instruction" is of the utmost importance.

Medical schools and hospitals are facing a critical shortage of dogs and cats for experimental purposes. This is not a simple matter of fund raising or of passing financial difficulty. Animals are simply not available. It is incongruous that this situation should obtain while thousands of animals are destroyed annually in the public pounds. These animals, vagrants and strays, are condemned to death as a menace to the health of the community. How much better that some of them should have death deferred until under humane auspices they are used for studies contributing to the health and welfare of humanity and of animal pets!

A hearing on S. 264 will be conducted before the Committee on Legal Affairs at the Gardner Auditorium at the State House in Boston on Tuesday, February 24, at 10:30 a.m. It is a matter of the greatest importance that legislators be informed of the urgent and cogent reasons for the passage of this bill.

The Constitution of the Commonwealth, in Section II of Chapter V, states: "Wisdom and knowledge, as well as virtue, diffused generally among the body of the people, being necessary for the preservation of their rights and liberties; and as these depend on spreading the opportunities and advantages of education in the various parts of the country, and among the different orders of the people, it shall be the duty of legislatures and magistrates, in all future periods of this commonwealth, to cherish the interests of literature and the sciences, and all seminaries of them. . . ."

A ROSE BY ANY OTHER NAME

THE ability to smell has been under investigation in New Haven, and certain revolutionary discoveries in this direction have been released by the Yale University News Bureau. The sensation of smell, apparently, does not come from chemical reactions set up within the olfactory organ by odorous substances that impinge upon it, but results rather from impulses sent out from the organ at extremely high frequencies, as from a radio transmitting station. Smell, because of highly scientific researches made with the common cockroach and the busy bee, has moved into the realm of radiation physics.

The high-frequency impulses emanating from the olfactory end organ, like one-way radar waves, fall within a detectable range of 8 to 14 microns. Substances falling outside this range — such, presumably, as carbon monoxide — cannot be smelled by human beings.

The theory of this new concept of smelling is based on the idea that heat moves toward a source of coolness. The olfactory organ is "hot"; the odorous gas is "cool." As the sense organ loses heat the gas gains it; when a balance is reached we become insensitive to the odor. Further work is expected to establish a smell spectrum in which the four thousand to six thousand odors detected by the human nose can be plotted. Thus the guesswork can be removed from smelling.

Smelling distances have apparently not yet been measured, and such naïve predictions as "smelling to high Heaven" will presumably remain in the realm of the unexplored. Nor has the intransitive form of the verb received its full share of scientific recognition. Studies on the ability to smell in this sense remain commercial and seem still to be restricted to those exquisites of radio pronouncement, the foghorn voices that, in a perfectionism of vulgarity, suggest the employment of certain cleansing mediums in the interest of social acceptance.

MASSACHUSETTS MEDICAL SOCIETY

MASSACHUSETTS MEDICINE AND THE ANIMAL

Antivivisectionism has flourished in Massachusetts for many years. All the requirements for such a situation prevail in eminent degree within the Commonwealth. We have three medical schools, an antivivisection society or two and no less than three Hearst newspapers.

Repeated and often frenzied efforts to obtain the passage of legislation restricting or abolishing animal experimentation have been defeated. With the type of intelligent lawmaker now prevailing on Beacon Hill it can be safely stated that antivivisectionist legislation will continue to be defeated.

Experimental animals, never adequate in number, have been increasingly difficult to obtain. Important wartime medical-research projects were delayed and were completed only with the greatest difficulty. The supply of laboratory animals has recently approached the vanishing point, and many vital research projects have been brought to a standstill. The progress of medical teaching and research in Massachusetts is seriously jeopardized.

Millions of dollars have been poured into our hospitals and medical schools. Generous funds have been made available for important research studies. Students, graduate students and patients come to us from considerable distances for what benefits Massachusetts medicine has to offer. This entire structure is endangered if animals in adequate number are not made available for the continuance of medical progress.

It is often difficult for the scientific mind to realize the violent feelings that possess the ardent antivivisectionist. Unless one is exposed twice daily and once on Sunday to the diatribes of the Hearst press and unless the reams of "literature" from the antivivisectionist societies are read it is difficult to realize the impassioned opposition generated by years of unchecked vituperative invective.

Some samples from editorials in the Boston Hearst newspapers follow: " . . . butchery — stolen pets literally cut to pieces from wagging tail to lapping tongue — crying out in excruciating agony — cutting . . . slashing . . . hacking — no anesthesia to ease the pain, no sympathy, no mercy — unspeakably brutal activities of the vivisectionists — slash off the dog's tail — gouge out his eyes — rip out his tongue." These are not confessions of an American opium eater. They are the considered opinion of a group of newspapers in Boston concerning our teachers in the medical sciences, our students in Massachusetts medical schools and all Massachusetts physicians trained under the requirements of animal experimentation.

The true antivivisectionist should be willing to forego such things as surgery, the sulfonamides, penicillin, streptomycin, immunization and the use of blood plasma and blood transfusion and the whole host of procedures derived from animal experimentation. Logically, our opponents should also protest our increasing use of chick embryos for the study of virus diseases. If the unborn human fetus has rights before the law the exaltation of the animal should force the antivivisectionists to protect the unborn chick.

A *Boston Daily Record* editorial on November 19, 1947, discussed the raising of funds for a hospital medical staff "for research into cancer, tuberculosis and other chronic diseases." The writer then pontifically stated:

> The medical fund raisers are going to meet more and more refusals from those who would normally subscribe, but who do not want to be placed in the position of subsidizing vivisection or other animal torture. Vivisectors must be taught that this country is against their merciless abuse of medical privilege. . . . Millions for mercy but not one cent for torture!

No suggestion is offered concerning a means of curing the diseases mentioned without recourse to experiments on animals. There is grave doubt that an infusion of printer's ink from Hearst editorial pages would have any effect in the treatment of these diseases. You don't have to be completely misinformed to be a Hearst editorial writer. But it certainly helps.

The task of refuting the various "*exposés*" and attacks of the opponents of animal experimentation is truly Augean. In March, 1947, the Hearst press publicized a matter involving an obscure biologist at William Jewell College in Liberty, Missouri. A campus pet dog named "Brownie" was chloroformed, and the dead body used for anatomic demonstration. The professor was hung in effigy, and "cruelty in the name of science" was protested.

Again in July, 1947, the Hearst press reported "Head of Medical School Denounces Vivisection." It seems that a course on animal surgery was abolished at the Mexican National School of Medicine because its educational value was stated to be poor. Dr. Herrejon, director of the school, did say:

> Without animals no physiology can be taught and without physiology no medicine can be learned. Medical scientific progress and its benefits to humanity cannot be deterred by misplaced pity to animals. As between animals and man we have chosen man . . . .

A review of the antivivisectionist publications or of their membership-campaign advertisements in the press shows persistence of all the old charges: "cruelty — torture — pet stealing." The quotations of a few long-deceased or misinformed churchmen are reiterated. These have about the same validity as the average physician's views on antidisestablishmentarianism.

There is egregious disregard of evidence and fantastic illogic of thought. George R. Farnum, Esq., president and counsel of the New England Anti Vivisection Society and editor of *Living Tissue*, is quoted in the Hearst *Boston American* of January 26, 1948, as stating:

> No one who knows anything about the practice of vivisection can deny that it involves suffering of the most

> excruciating kind. . . . Yet after long years it is admitted that no real progress has been made. If anything has been proved, it is the utter futility of all this shocking cruelty.

This is the same profound thinker who observed at a State House hearing a year ago:

> Insulin is a dangerous thing. A man who becomes addicted to it is a slave, more or less, to the continuous treatments and all that. Some people assert that it has a very deleterious effect. The statistical tables are contradictory about it.

In the January, 1947, issue of *Living Tissue* appeared an interesting item captioned "The Oxford Case":

> A sordid incident which should be "prescribed reading" for those who ignore the evils of vivisection and naïvely trust the word of those who defend it, is reported from no less a [sic] famous institution of learning and citadel of culture than Oxford University. It seems that Edward George Tandy Liddell, Professor of Physiology, was convicted of cruelty to cats. *His appeal was disallowed* [italics mine]. Excerpts from a commentary on the case which appeared in the November issue of the English publication, *The Cat*, follow.

The excerpt stated that Professor Liddell was charged and convicted in May of cruelty to some thirty-six cats. The R.S.P.C.A. was congratulated for prosecuting and winning the case.

A review of four clippings from the London *Times* helps to freshen the air. The last of these, under date of October 11, 1946, is most significant. It states that "none of the allegations at the Oxford City Quarter Sessions was proved against Dr. Liddell except that of overcrowding and, therefore, he (The Recorder) would reduce the fine of £25 imposed by the city magistrates to £5." Even this patent sop to the antivivisectionists hardly warrants the language used in *Living Tissue*.

The New England Anti Vivisection Society has a particular fondness for quoting "the late Dr. Henry J. Bigelow, Professor of Surgery at Harvard Medical School and long associated with the Massachusetts General Hospital." The "late" Henry Jacob Bigelow (1818–90), speaking of animal experimentation as he observed it at the Veterinary School at Alfort, France, some thirty years before the advent of ether anesthesia, stated before the Massachusetts Medical Society on June 7, 1871, "There will come a time when the world will look back to *modern* [italics mine] vivisection in the name of science as they now do to burning at the stake in the name of religion." The blithe disregard for the dictionary definitions of such terms as "late," "cruelty" and "torture" is rather characteristic of our opponents.

Another look at the record is in order. The "late" Dr. Bigelow wrote a letter to *Our Dumb Animals*, the publication of the M.S.P.C.A. This letter stated "The dissection of an animal in a state of insensibility is no more to be criticized than is the abrupt killing of it, to which no one objects. . . . A painless experiment upon an animal is unobjectionable."

His son, William Sturgis Bigelow, wrote in a letter to the Editor of the *Boston Herald* on December 13, 1921:

> My father was extremely active in securing the physiological laboratory for Harvard University. He did as much as anybody to secure that very laboratory, where then, and now, animal experimentation is carried on when necessary and where results have been obtained which have been of vital benefit to the human race.

The dentist Morton first tested ether on his dog. Walter B. Cannon, pioneer in x-ray examination of the alimentary tract, worked with a bismuth salt on cats. The surgery of Elliott C. Cutler on the valves of the heart and the work of Lennox in epilepsy, of Gross in congenital heart defects and of Harken in wartime wounds of the heart and great vessels would have been impossible without the contributions of animal research in Massachusetts.

Our opponents state that only relatively few physicians have any stake in animal experimentation. This clever "divide and rule" stratagem must be strongly opposed. In our writings the background of animal studies should be stated. Our speakers must stress this vital subject. And above all our patients must be informed. It takes but a moment to tell the animal background of such drugs as digitalis, adrenalin, Dilantin and the rest.

A bill has been filed before the Massachusetts legislature. The Nolen–Miles Pound Law, Senate Bill 264, is pending before the Committee on Legal Affairs. This bill will make unclaimed and unredeemed animals from public pounds available for medical teaching and research. Pets given over to animal pounds for execution are excluded from the provisions of the bill. The six-day period provided by law for the recovery of lost pets is maintained.

Relatively few of the thousands of dogs and cats executed annually in local pounds are required by our medical schools and hospitals. These will be humanely treated. It is their privilege to serve as the K9-corps dogs did in wartime — for the protection of their human masters. Benefits will be obtained that are for the preservation of life and the relief of suffering of both man and animal.

We have repeatedly justified our conduct of the priceless privilege and heritage of animal experimentation. No law has been passed to restrict our humane teaching and research. We can no longer continue our necessary work without extreme difficulty and unwarranted expense. We appear before the legislature with clean hands and unselfish motives.

Our opponents profess to be humanitarians. They would protect and benefit the dog and cat. Our higher humanitarian sentiments must prevail. We protect and benefit the dog, the cat and the human being.

JOHN F. CONLIN, M.D.
Director of Medical Information and Education, Massachusetts Medical Society; chairman, Massachusetts Committee for Medical Research.

NOTICES

ANNOUNCEMENT

Dr. Nazareth Adzigian, having completed military service, announces the opening of his office for the practice of general medicine at 19 Cliff Road, Wellesley Hills.

NEW ENGLAND DIABETES ASSOCIATION

A clinical meeting will be held under the auspices of the New England Medical Center on Wednesday, February 18, at 7:30 p.m. in the auditorium of the Joseph H. Pratt Diagnostic Hospital.

PROGRAM

Education of the Diabetic Patient: A tribute to Frances Stern. Joseph Rosenthal, M.D.

Intermittent Claudication. Samuel H. Proger, M.D.

Diabetes as a Manifestation of a Systemic Disease. David Hurwitz, M.D.

Glycogen-Storage Disease. Richard Wagner, M.D.

There will be an opportunity for discussion of each paper.

AMERICAN TRUDEAU SOCIETY

Four evening meetings will be held in conjunction with the Postgraduate Course in Thoracic Diseases, to be held by the American Trudeau Society in April, as advertised elsewhere in this issue of the *Journal*. These meetings will be held at the Boston Medical Library at 8 p.m.

PROGRAM

Wednesday, April 7. Factors Involved in Dyspnea as it Develops in Pulmonary Disease. Dr. George W. Wright, of the Trudeau Foundation.

Friday, April 9. Streptomycin in the Treatment of Tuberculosis. Dr. John B. Barnwell, chief, Tuberculosis Division, Veterans Administration, Washington.

Wednesday, April 14. The Importance of Establishing the Etiology of a Pulmonary Disease before Initiating Treatment. Dr. David T. Smith, professor of bacteriology and associate professor of medicine, Duke University School of Medicine.

Friday, April 16. B. C. G. Vaccination in All Age Groups. Dr. Sol Roy Rosenthal, assistant professor of bacteriology and public health, University of Illinois College of Medicine.

Physicians, medical students, nurses and others interested in the subject are cordially invited to attend *without charge*.

GREATER BOSTON MEDICAL SOCIETY

The February meeting of the Greater Boston Medical Society will be held in the auditorium of the Beth Israel Hospital on Tuesday, February 17, at 8:15 p.m.

The subject will be a symposium on psychosomatic medicine. Dr. Felix Deutsch will speak on "The Use of the Psychosomatic Concept in Medicine," and Dr. Jacob E. Finesinger on "Psychotherapeutic Procedures in Peptic Ulcer."

AMERICAN ACADEMY OF PEDIATRICS

The areal meeting of the American Academy of Pediatrics will be held at the Hotel Statler, Buffalo, New York, from April 29 to May 2.

Members of state medical societies are invited to attend. The registration fee will be $5.00 for such nonmembers of the Academy. This is in addition to the regular $5.00 registration fee for members, making a total of $10.00 for nonmembers of the Academy. This fee includes a ticket to the banquet.

Registration may be made ahead of time by application to Dr. C. G. Grulee, secretary-treasurer, American Academy of Pediatrics, 636 Church Street, Evanston, Illinois, enclosing a check for $10.00 or registration may be at the time of the meeting.

ATOMIC ENERGY COMMISSION FELLOWSHIP TRAINING PROGRAM

The Atomic Energy Commission, through its Division of Biology and Medicine, announces a Fellowship Training Program in the field of atomic energy as applied to biology and medicine. This program includes training for doctors of medicine and will be administered for the Commission by the National Research Council. Further detailed announcements will be forthcoming in the immediate future. It is hoped that sufficient interest will be exhibited for the first group of fellows to begin training on September 1, 1948.

The fellowships will be awarded to physicians who have completed an internship or residency and will be of two years' duration. There will be a liberal stipend, consideration being given to the marital status of the fellows. Training will include formal instruction in such essential subjects as chemistry, biology, physics and mathematics, with emphasis on their application to atomic energy in medicine. After the attainment of a well rounded background in these sciences, it is anticipated that the fellows will spend the remainder of their fellowship in basic and regional clinical research at the various laboratories that are a part of the Commission and where there are unique opportunities for such endeavor. So far as possible, the fellows will be allowed a choice of their training sites and the research problems undertaken.

At the termination of such training the fellows will be free to follow careers of their own choice. However, opportunities will be available for continued employment in the medical facilities of the Atomic Energy Commission where there are active and extensive programs in atomic energy as it applies to the various phases of medicine, both fundamental and clinical.

The rapid development of atomic energy in the field of biology and medicine indicates a vast opportunity for study and development in this branch of science. The Atomic Energy Commission is anxious to further the use of atomic energy in medicine, and it is believed that a fellowship program as outlined will be valuable to all concerned.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, FEBRUARY 19

THURSDAY, FEBRUARY 19
12:00 m. Medical Staff Meeting. Nurses Home, Allerton Hospital, Brookline.

FRIDAY, FEBRUARY 20
*9:00–10:00 a.m. Physiological and Pharmacological Factors on Gastric Secretion. Dr. Byron B. Clark. Joseph H. Pratt Diagnostic Hospital.
*10:00 a.m.–12:00 m. Medical Staff Rounds. Peter Bent Brigham Hospital.

MONDAY, FEBRUARY 23
12:00 m. Clinicopathological Conference. Margaret Jewett Hall, Mt. Auburn Hospital, Cambridge.
*12:15–1:15 p.m. Clinicopathological Conference. Peter Bent Brigham Hospital.

TUESDAY, FEBRUARY 24
12:00 m. X-Ray Conference. Margaret Jewett Hall, Mt. Auburn Hospital, Cambridge.
*12:15–1:15 p.m. Clinicoroentgenological Conference. Peter Bent Brigham Hospital.
*1:30–2:30 p.m. Pediatric Rounds. Burnham Memorial Hospital for Children, Massachusetts General Hospital.

WEDNESDAY, FEBRUARY 25
*9:00–10:00 a.m. The Clinical Aspects of Surgery of the Extrahepatic Biliary Tract. Dr. Norman J. Wilson. Joseph H. Pratt Diagnostic Hospital.
*12:00 m. Grand Rounds and Clinicopathological Conference (Children's Hospital). Amphitheater, Peter Bent Brigham Hospital.
*2:00–3:00 p.m. Combined Clinic by the Medical, Surgical and Orthopedic Services. Amphitheater, Children's Hospital.

*Open to the medical profession.

JANUARY–APRIL. Thirteenth Postgraduate Seminar in Neurology and Psychiatry. Metropolitan State Hospital. Page 348, issue of August 28.
FEBRUARY 17. Greater Boston Medical Society. Notice above.
FEBRUARY 18. New England Diabetes Association. Notice above.
FEBRUARY 23–25. American Hospital Association. Page 136, issue of January 22.
FEBRUARY 23–28. Postgraduate Assembly in Endocrinology. Page 36, issue of January 1.

(*Notices concluded on page xiii*)